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Archives of Dermatology and Syphilology

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THE DEXTROSE AND WATER CONTENT OF NORMAL AND OF INFLAMED SKIN

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AND
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PHILADELPHIA

The present study has been undertaken as part of a general investigation of the influence of carbohydrate metabolism on the normal and on the diseased skin. As suggested in an earlier paper,[1] it would seem probable that the final answer to the moot question among clinicians as to whether a high or low carbohydrate intake has any effect on the skin will be found in a more thorough understanding of the skin itself. It can be stated definitely that most dermatoses are not accompanied by any derangement of the carbohydrate metabolism of the patient, as indicated by studies of the blood sugar during fasting and dextrose tolerance.[2] This evidence does not, in our opinion, answer the question as to whether there is any derangement of the carbohydrate metabolism of the normal or diseased skin of the patient.

This question has been the subject of an increasing number of studies, notably those of Rost [2b] and of Urbach and Wohlgemuth and their co-workers.[3] These have previously been summarized by one of us; and it would not be possible within the limits of this paper to review the entire subject to date.

The dextrose content of experimentally inflamed skin has been studied, so far as we are aware, in only one investigation, that of

From the Department of Physiological Chemistry (D. Wright Wilson, Ph.D., Director) and the Department of Dermatology and Syphilology (John H. Stokes, M.D., Director), University of Pennsylvania School of Medicine.

1. Pillsbury, D. M.: The Intrinsic Carbohydrate Metabolism of the Skin, J. A. M. A. **96**:426 (Feb. 7) 1931.

2. (*a*) Schamberg, J. F., and Brown, Herman: The Chemistry of the Blood in Diseases of the Skin: A Study of Eight Hundred and Seventy-Five Cases, Arch. Dermat. & Syph. **21**:1 (Jan.) 1930. (*b*) Rost, G. A.: Hyperglycemia and Skin Diseases, Brit. J. Dermat. **144**:57 (Feb.) 1932.

3. Urbach, E., and Sicher, Grete: Der Zuckergehalt der Haut unter physiologischen und pathologischen Bedingungen, Wien. klin. Wchnschr. **41**:1481 (Oct 25) 1928; Beiträge zu einer physiologischen und pathologischen Chemise der Haut, Arch. f. Dermat. u. Syph. **157**:160, 1929. Wohlgemuth, V., and Sugihara, N.: Die Fermerte der Haut, Biochem. Ztschr. **163**:260, 1925. Yamasaki, Y.: Ueber die Fermente der Haut, ibid. **147**:203, 1924. Ottenstein, Berta: Untersuchungen über den Gehalt der Haut und des Blutes an diastatischem Ferment und dessen biochemische Bedeutung bei Hautkrankheiten, ibid. **240**:328, 1931.

Miyake and Narahara.[4] Miyake and Narahara studied the sugar curves of normal and irritated skin and of the blood in rabbits that had received dextrose. They noted a lessened sugar tolerance in rabbits with extensive dermatitis. They concluded that inflamed skin commonly shows varying changes in its capacity for storing dextrose. They found that the residual normal skin in dermatitic rabbits functioned normally, as indicated by the skin sugar curve, but that the irritated skin did not show the slightest correlation with the normal. They noted no relation between the lessened dextrose tolerance of markedly dermatitic animals and the erratic dextrose curves of inflamed skin.

We have studied the dextrose and water content of normal and dermatitic skin, the effect of hyperglycodermia on the water content of normal and inflamed skin and the dextrose content of inflammatory crusts and of the epidermis. Our interest in the water content of skin was stimulated by the frequent observance of eczema in fat infants with marked turgor of the skin, many of whom were being given high carbohydrate diets, and by the recent study of McClendon[5] indicating marked water retention following ingestion of dextrose in adult subjects. McClendon believes that the skin participates in this water retention. Bischoff and Voit[6] long ago reported an increased water content of all the organs of animals fed an exclusively carbohydrate diet, and Tobler and Bessau[7] observed an increased water content of the skin in infants fed entirely on carbohydrate.

Urbach has argued the advisability of expressing the dextrose content of tissue in terms of dry weight of the tissue. We felt that in a study of inflamed edematous tissue, data on the dry weight should be available for comparison.

METHOD

Dextrose determinations were done by the Hagedorn-Jensen[8] method. The use of this method in determinations on tissue was first suggested by Urbach and Fantl,[9] but we were not entirely convinced of its reliability and undertook a critical study of it before the work reported here was begun. The method consists of a direct adaptation of the Hagedorn-Jensen method of determination of

4. Miyake, I., and Narahara, K.: Eczematöse Hautveränderung und Zuckerstoffwecksel: Hautzucker und eczematöse Hautveränderung, Jap J. Dermat. & Urol. **30**:85, 1930.

5. McClendon, J. F.: On the Relation of Blood Sugar to Blood Volume, and Carbohydrate to Water Retention, Am. J. Physiol. **98**:216 (Sept.) 1931.

6. Bischoff, T. L. W., and Voit, Carl: Die Gesetze der Ernährung des Fleischfressers durch neue Untersuchungen festgestellt, Leipzig, C. F. Winter, 1860.

7. Tobler and Bessau: Allgemeine pathologische Physiologie der Ernährung und des Stoffwechsels im Kindesalter, Wiesbaden, 1914.

8. Hagedorn, H. C., and Jensen, B. H.: Zur Mikrobestimmung des Blutzuckers mittels Ferricyanid, Biochem. Ztschr. **135**:46, 1923.

9. Urbach, E., and Fantl, P.: Methoden zur quantitativ-chemischen Analyse der Haut, Biochem. Ztschr. **196**:471, 1928.

blood dextrose to tissue. Finely sliced portions of skin were placed in a test tube containing 5 cc. of 0.45 per cent zinc sulphate and 1 cc. of tenth-normal sodium hydroxide. The tube was weighed to 1 mg. immediately before and after the addition of the tissue. The weight of the tissue varied from 0.1 to 0.15 Gm. The tubes were placed in a boiling water bath for exactly three minutes and the contents filtered through washed cotton which was rather tightly packed into the tube of a small glass funnel. The precipitate was washed twice with 3 cc. portions of hot distilled water. The dextrose content of the filtrate was then determined by the Hagedorn-Jensen ferricyanide method as modified by Cole.[10]

In the preliminary study of the method two possible sources of error which were not discussed by Urbach and Fantl were investigated: first, whether or not the treatment of the tissue for three minutes in the boiling water bath was sufficient to extract all the dextrose, and second, what proportions of the extracted reducing materials represented dextrose. Folin, Trimble and Newman,[11] working with skin, and Bischoff and Long,[12] working with muscle, extracted the tissue for one hour or more. In neither of these investigations was the Hagedorn-Jensen method used.

This study of the method, which is being reported elsewhere,[12a] indicated that virtually all of the dextrose is extracted within three minutes from fine strips of skin at boiling temperature, and that the considerably higher reducing values obtained with the Hagedorn-Jensen reagent on extraction for periods up to an hour were due almost entirely to nonfermentable reducing substances. Comparison of the results obtained on skin from the same animal by the Hagedorn-Jensen method and by the Somogyi[13] method of precipitation with determination of the reducing values by the Shaffer-Hartman[14] technic showed satisfactory agreement. Our data indicated that the nondextrose reducing portion of the determination by the Hagedorn-Jensen method varied between 10 and 20 mg. per hundred grams of tissue, calculated as dextrose. With careful technic the factor of error of the method did not exceed ± 5 mg. per hundred grams. This is not as good as the results with blood, in which variations no greater than ± 1 mg. per hundred cubic centimeters were noted. All determinations were made in duplicate.

The method is not difficult, it may be carried out rapidly and it possesses the advantages of a micromethod, which is indispensable in a study of this type.

The water content of the skin was determined by weighing approximately 0.5 Gm. of skin in a closed weighing bottle, drying it for forty-eight hours at 105 C. (221 F.) and reweighing it.[15] Comparison of this method with drying at

10. Cole, S. W.: Practical Physiological Chemistry, Baltimore, Williams & Wilkins Company, 1926.

11. Folin, Otto; Trimble, H. C., and Newman, L. H.: The Distribution and Recovery of Glucose Injected into Animals, J. Biol. Chem. **75**:263 (Oct.) 1927. Trimble, H. C., and Carey, B. W.: The True Sugar Content of the Skin in Diabetes, Arch. Dermat. & Syph. **25**:6 (Jan.) 1932.

12. Bischoff, F., and Long, M. L.: The Depletion of Muscle Sugar by Adrenalin, J. Biol. Chem. **87**:47, 1930.

12a. Pillsbury, Donald M., and Kulchar, George V.: The Use of the Hagedorn-Jensen Method in the Determination of Skin Glucose, J. Biol. Chem. **106**:351 (Aug.) 1934.

13. Somogyi, M.: Method of Sugar Determination, J. Biol. Chem. **70**:599 (Nov.) 1926.

14. Shaffer, P. A., and Hartman, A. F.: Iodometrin Determination of Copper and Its Use in Sugar Analysis, J. Biol. Chem. **45**:363 (Jan.) 1921.

15. Herrmann, F.: Ueber die Wasserbindung in der Haut, Ztschr. f. d. ges. exper. Med. **76**:780, 1931.

37 C. (98.6 F.) in a partial vacuum over phosphorus pentoxide did not reveal significant differences. Considerable variation in duplicate determinations was noted initially. Adolph, Gerbasi and Lepore [16] have reported variations exceeding ± 4.5 per cent in dog skin. With careful attention to close and even shaving of the skin and by making certain that no subcutaneous tissue was adherent to the samples, the latter condition possible of fulfilment only in rabbits in our experience, the factor of error of the method was reduced to approximately ± 1 per cent. The tissue must be rapidly removed from the animal and quickly placed in a closed weighing vessel if marked losses of water are to be avoided. Specimens with adherent extravasated blood should not be used.

We have found that rubbing of the skin with gauze soaked in benzine is a satisfactory method of irritation. The degree of resultant irritation is dependent on the time and vigor of the rubbing. Samples of skin in which crusting had occurred were not used for water determination. The use of croton oil or cantharides plaster gave rise to spurious reducing values.

Rabbit skin was used throughout. Sodium amytal anesthesia (75 mg. per kilogram intraperitoneally) was employed in obtaining the specimens of skin. The animal was not tied until complete anesthesia had occurred. Close shaving of the skin was done forty-eight hours previous to the experiment.

RESULTS

Specimens of skin from nonfasting rabbits were removed from normal and from inflamed areas for both dextrose and water determination. The results are given in the table.

The Dextrose and Water Content of Normal and Inflamed Skin (Nonfasting Animals) *

	Normal Skin		Inflamed Skin	
Experiment	Dextrose, Mg. per 100 Gm.	Water, per Cent	Dextrose, Mg. per 100 Gm.	Water, per Cent
XL	194	71	198	75
XLII	80	75	78	77
XLIII	135	73	160	76
			(48 hrs.) 160	73
XLIV	...	71	...	76
				(3 hrs.) 74
XLVII	224	68	(½ hr.) 223	72
			(1 hr.) 223	72
			(48 hrs.) 212	68
LXVI	169	74	152	77
LXVII	179	67	195	68
LXVIII	140	69	155	71
LXXI	130	72	126	75
LXXII	...	66	...	70
LXXIII	129	69	140	69
LXXIV	132	71	149	76
	140	..	(3 hrs.) 138	74
LXXVII	135	..	142	..
LXXIX	189	..	170	..

* Specimens of inflamed skin were taken twenty-four hours after irritation, unless otherwise indicated.

The water content of inflamed skin tends to be higher than that of normal skin. The increase did not exceed 4 per cent in any case. There

16. Adolph, E. F.; Gerbasi, M. J., and Lepore, M. J.: Redistribution of Water Measured in Blood and Tissues, Am. J. Physiol. **101**:1 (May) 1932.

is no indication that the dextrose content of the skin changes markedly following experimental irritation. In only four experiments could the variation between the dextrose content of normal and that of irritated skin be regarded as significant; in two of these there was an increased value in the irritated skin, and in two a decreased value.

We have attempted to determine whether or not the injection of large amounts of dextrose in nonfasting animals produced any change in the water concentration of the skin, and whether or not there was any variation in the increase in dextrose in the normal and irritated skin. The results of these experiments may be summarized briefly. The water content of normal rabbit skin was determined before and after injection of dextrose in ten animals; in two there was an increase and in two a decrease, and six showed no change (a variation of 2 per cent was not regarded as significant). The water content of irritated skin was determined before and after injection of dextrose in six animals; in two there was a decrease and in four an increase, with no specimens showing no change. In ten animals which had received dextrose intraperitoneally, comparison of the dextrose contents of the irritated and normal skin showed a definitely higher content in the irritated skin in six animals, a lower content in two and no variation in two.

The dextrose content of the epithelium was obtained by slicing very thin Thiersch grafts from the surface with a razor blade. The removal caused either no bleeding or only an occasional small bleeding point, indicating that the section infrequently went as deep as the papillae. The crust was obtained either by scraping the surface of the inflamed skin or by stripping pieces of crust off with thumb forceps.

The dextrose content of the epidermis showed a significant increase of 16 mg. per hundred grams over that of the whole skin in only one of the four determinations made. The reducing substances of inflammatory crust, however, were consistently high. Determinations made on a series of eight nonfasting animals showed the reducing substances in the normal skin to average 162 mg. per hundred grams, while those in the inflammatory crust averaged 408 mg. Determination of the nonfermentable reducing substances in the crust in three animals showed an increased proportion of this material; the fermentable dextrose, however, was still from two to three times that of the underlying skin.

In this connection mention should be made of an observation the possible significance of which did not occur to us until near the completion of our experiments. In rabbits with inflamed skin into which injections of dextrose had been made, a high incidence of infection of the irritated sites was evidenced by the formation of a yellow impetigo-like crust, with considerable underlying free pus. In rabbits which had

not received large quantities of dextrose the skin usually healed with little evidence of infection. This observation is being investigated further.

COMMENT

No significant variation in the dextrose content between normal and inflamed skin was noted in rabbits fed a normal mixed diet. The water content of inflamed skin was only slightly higher than that of normal skin in rabbits which had not fasted and in those which had received dextrose. In many cases the change was barely outside the experimental error of the method, although consistently tending toward a higher level in the inflamed skin. This relatively moderate increase was a matter of surprise to us, in view of the gross appearance of the tissue. All the samples of inflamed skin were notably edematous and thickened and were usually of an almost gelatinous consistency on cutting. Two possible explanations of the only moderate increase in water concentration occurred to us: first, that there was a marked concomitant increase in solids due to cellular or protein influx, and second, that some of the water in the skin may have been present in loosely bound chemical combinations. It was with the latter possibility in view that we undertook the drying of samples over phosphorus pentoxide in a partial vacuum. The water content as determined by this method showed no variation from that determined on duplicate samples by drying at 105 C. Samples were also dried at temperatures up to 125 C. (256.8 F.), with no increase in water loss.

We did not observe marked increase in the water content of normal and inflamed skin in which the dextrose content had been raised experimentally. Objection might be made to the injection of a hypertonic solution of dextrose intraperitoneally in interpreting this finding. In rabbits in which simultaneous determination of the blood sugar was made, however, no marked disturbance of the blood sugar-skin sugar ratio was noted when the samples were taken an hour or more after the injection of dextrose. In two experiments samples of skin were taken twelve and twenty-four hours, respectively, after the injection of dextrose, when water equilibrium in the various organs might well be assumed to have been established. We recognize that the conditions of this type of experiment are not those encountered in human beings or animals that have received a diet high in carbohydrates for long periods of time. The data do indicate, however, that simply a rapid marked increase in the dextrose content of the skin is not accompanied by an increase in the water concentration.

In animals in which the dextrose concentration of normal and that of inflamed skin were compared after the injection of dextrose, some variation was always noted in the dermatitic tissue, with a majority of the

samples showing a higher dextrose value in inflamed skin. This finding is in accord with that of Miyake and Narahara. There would seem to be some derangement in the power of inflamed skin to absorb dextrose following a sharp rise in the blood sugar. In this connection the observation of an increase in infected dermatitis in animals which had received dextrose should be kept in mind. These findings might be interpreted as having definite clinical significance.

Our results indicate a striking increase in the dextrose content of crusts as compared with the underlying inflamed skin or the normal skin of the same animal. We are of the opinion that this higher value may be explained on the basis of concentration of the dextrose during the drying of the exudate. It is probable that some of the dextrose is changed by enzymatic action, but it seems doubtful that this proceeds rapidly after the crust has become thoroughly dry. Diffusion of dextrose between the crust and the underlying skin must proceed slowly, if at all.

SUMMARY

1. The normal and the inflamed skin of the same animal receiving a normal diet do not show variation in the dextrose content.

2. The water concentration of the inflamed skin of the rabbit is only slightly greater than that of the normal skin.

3. The dextrose content of the inflamed skin following injection of dextrose commonly varies from that of the normal skin; as a rule, it is higher.

4. The dextrose content of the epidermis and that of the whole skin coincide closely.

5. The dextrose concentration of inflammatory crusts is high.

6. Infection of the irritated skin develops more commonly in rabbits in which dextrose has been injected than in those given normal mixed diets.

ABSTRACT OF DISCUSSION

DR. S. WILLIAM BECKER, Chicago: Chemical analysis of the skin presents considerable difficulty. The late Prof. Bruno Bloch was loath to undertake chemical studies of the skin, owing to the uncertainty of existing chemical methods. However, it is necessary for some to pioneer in this field, and Dr. Pillsbury has the courage and tenacity to devote his time and energy to this task. It is work of this kind that should assure American supremacy in scientific dermatology in the next few decades.

I should like to mention some work by Dr. Gersh of the Department of Anatomy of the University of Chicago. He has perfected an old method of microchemical study. Fresh skin is frozen in liquid air and desiccated in a vacuum at a low temperature. It is then impregnated with paraffin and is ready for sectioning. In this way all diffusion or chemical change is prevented, and accurate microchemical studies may be performed.

In the Section of Dermatology work is being done on the metabolism of fungi, and the same chemical methods, namely, those for lactic acid and dextrose, have been applied to the study of the skin. Dr. Ginsberg has perfected a method of extracting the skin, which his associates believe prevents glycogenolysis, inactivates enzymes and does not result in the formation of reducing substances. The work has been largely on the skin of dogs, which were readily available. Dog skin was found to contain half as much dextrose as is present in rabbit skin. The results with rabbit skin correspond with those of Dr. Pillsbury, although my associates and I have carried out only a few determinations. Dr. Ginsberg's method of extracting the skin consists in freezing the specimen in liquid nitrogen and pulverizing it by one or two heavy blows by a sledge-hammer in a specially constructed apparatus. The resulting powder is poured into a flask containing the extracting substance.

Dr. Jeffrey C. Michael, Houston, Texas: This work seems quite abstruse, but certain practical results are coming from such studies. For instance, Perutz, as a result of studies on the water metabolism of the skin, proposed a method of treating widespread acute dermatitis by a salt-free diet and low water intake combined with small doses of phenobarbital and a diuretic. I have used the method in a few cases, with beneficial effects in two, but with no result in the others. Perhaps further experience or a better selection of cases will indicate the benefits and limitations of the method.

Dr. Donald M. Pillsbury, Philadelphia: I am much interested in the ingenious apparatus for grinding samples of skin that was demonstrated by Dr. Becker. Dr. Friedman deserves congratulation as the handling and grinding of skin with a pestle and mortar is a difficult and tedious process. In our preliminary work we did a number of dextrose determinations on frozen skin to ascertain whether any appreciable change in the dextrose content occurred during the two to four minutes necessary to transfer the samples of skin from the animal to the water bath. We found no appreciable change during this time. The possibility of hydrolysis in the water bath was likewise carefully studied.

It is admitted that the rabbit is a highly volatile animal as regards its carbohydrate metabolism. Precautions were taken to avoid struggling. The animal was not tied during the intraperitoneal administration of the amytal and was allowed to rest quietly in its cage until complete anesthesia had occurred. In spite of this we believe that resting values in the rabbit must be very carefully interpreted, and it will be noted that we have based our conclusions on a comparison of values obtained on tissue from the same animal removed at the same time.

Apropos of Dr. Michael's remarks, I have in mind a recent study by Herrmann in which he demonstrated that the ingestion of salt has considerable influence on the water metabolism of the skin. It is apparent that as yet we know little about the changes in water in the skin. It is to be hoped that isolated studies such as ours can eventually be pieced together with those of other workers in the field of chemistry of the skin to make an understandable and possibly useful whole.

URINARY PROTEOSE IN ECZEMA

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The recent reports of Oriel and Barber [1] on urinary proteose in allergic disorders have created a new intense interest in a group of conditions the etiology of which is obscure and which are usually resistant to treatment. The claim of these authors to have demonstrated in the urine of allergic patients the specific causes of their maladies seems partially to have resolved a perplexing sector of medicine into something simple enough for one who is not a specialist to comprehend. And more than this, in demonstrating the cause, they have provided, at arm's length, the cure for each of the afflicted persons. The proteose in the urine of every allergic person, according to their studies, is individualistic, and apparently cannot be interchanged successfully with that from the urine of another patient even if both come from the urine of persons with the same disorder. With their report, allergy seems one milestone closer to solution.

The mechanism of allergy has had its cycles of various theories. There was the one of anaphylatoxin enunciated by Friedberger,[2] which assumed the production of a poisonous principle in the allergic reaction. Then came the theory of protein cleavage, which later was generally abandoned. Another assumption was the detoxification of serum protein, and, last, the one of colloidal precipitation. The thought-clock of allergic phenomena appears now to be turned back with the stream of recent reports on urinary proteose. The previously abandoned theory of protein cleavage seems to have gained new life and plausibility. Whether or not all this will sufficiently substantiate the theory of protein cleavage remains to be seen. Certainly the new evidence upholding it will have

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Read before the Section on Dermatology and Syphilology, at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 14, 1934.

1. Oriel, G. H., and Barber, H. W.: Proteose in Urine Excreted in Anaphylactic and Allergic Conditions, Lancet **2**:231 (Aug. 2) 1930; Urinary Proteose, ibid. **43**:424, Brit. M. J. **2**:60 (Sept. 5) 1931.

2. Friedberger, E.: Weitere Untersuchungen über Eiweissanaphylaxie: IV. I. Das Anaphylaxiegift (Anaphylatoxin), Ztschr. f. Immunol. u. exper. Therap. **4**:636, 1909.

to be unusually strong, because there are some grave objections to the tenability of this theory.

HISTORICAL REVIEW

Reports of the "ether reaction" of urine appeared in the literature about forty years ago without receiving much comment. Plosz,[3] in 1890, showed that when urine is strongly acidified with acetic acid and shaken with ether, chloroform or amyl alcohol, the mixture on separating forms two layers, and on the boundary between the two a gummy, waxy scum appears which is protein in nature. Plosz remarked that such a reaction is given by all urine, and concluded from this that all urine contains protein. He found that the material which he obtained from urine is not a homogeneous substance, since it is only partly soluble in acetic acid and partly soluble in water, alkali and strongly concentrated solutions of sodium chloride. Plosz felt that because the material did not dissolve in acetic acid, but dissolved in dilute alkali, only to be precipitated on the addition of acetic acid, it behaved like mucin. Plosz concluded that the material which he obtained from urine by the ether reaction always contained protein and a substance which acted like mucin.

Mörner [4] described a substance obtained from the urine of normal persons as well as from that of persons suffering from degenerative conditions, such as malignant diseases and tuberculosis. He thought that it was mucin derived from the urinary passages, and that it had not passed through the kidneys.

Smith,[5] in 1892, described a similar reaction of urine with ether: when acidified urine was shaken with ether, a thick scum appeared as the layers separated. He believed that the amount of scum that appeared was influenced by good appetite and good digestion and was markedly diminished after long fasting or when the diet was greatly restricted.

Oriel and Barber, in 1930,[1] in their studies on allergy and related conditions, paid particular attention to the urine of asthmatic persons, patients with eczema and other allergic persons, and found that when the acidified urine was shaken with one-fifth of its volume of ether, the mixture separated into two layers. The ether precipitate varied in extent and consistency according to whether the urine was derived from a healthy or an allergic person who at the moment was in a state of acute exacerbation of his disorder. When alcohol was added to the ether layer that contained the scum, a precipitate was obtained which

3. Plosz, P.: Untersuchungen über den Eiweissgehalt normalen Harns, Jahresb. u. d. Fortschr. d. Thierchem. **20**:215, 1890.

4. Mörner, K.: Untersuchungen über die Proteinstoffe und die eiweissfällenden Substanzen des normalen Menschenharns, Skandinav. Arch. f. Physiol. **6**:332, 1895.

5. Smith: The Reaction of Urine with Ether, Lancet **1**:688, 1892.

gave the biuret, Millon, Adamkiewicz and Molisch reactions. Oriel and Barber found that the precipitate obtained from the urine, especially that obtained during an attack, contained an antigen, which they felt was responsible for the attack, since skin reactions and a reproduction of the attack occurred when a solution of the precipitate was injected into the patient from whom it had been derived.

Since the original work of Oriel and Barber there have been many controversial reports from all over the world in quick succession.[6] Because of the difference in opinion about the material and the process by which it was obtained, we decided to undertake an investigation with a view to obtaining first-hand evidence for an opinion, and perhaps to throw some further light on the subject. We felt that the method of Oriel and Barber must produce an impure substance which did not yield clearcut results from skin tests that are meant to be performed with specific substances. We believed that purifying their product might help decide the debate.

PROCEDURE

The original method of Oriel and Barber was as follows: Five hundred cubic centimeters of urine was acidified with 5 cc. of 25 per cent sulphuric acid until the solution was acid to congo red; 100 cc. of ether was then added. The mixture was shaken vigorously in a stoppered separating funnel for a few minutes and then allowed to stand until the ether layer separated. The aqueous layer was then discarded, and 100 cc. of 95 per cent solution of alcohol was added to the ether layer. The precipitate was allowed to stand, was separated by centrifugation in sterile tubes and dried under sterile conditions. It was then dissolved in graduated quantities of tenth-normal sodium hydroxide to make the dilutions used in the tests. The diluting material was a solution containing 0.4 per cent phenol in physiologic solution of sodium chloride. The test dilutions were made by adding 1 cc. of the tenth-normal sodium hydroxide solution of the precipitate to 9 cc. of the solution containing 0.4 per cent phenol in saline solution, to make a dilution of 1:10, and so on.

We attempted to control the Oriel and Barber material by subjecting the urine from which it was obtained to a procedure accepted by biochemists, namely, the method of precipitation with ammonium sulphate. All specimens of urine and all tests were run parallel by both methods. Furthermore the ammonium sulphate precipitation was carried out on the filtrate ordinarily discarded in the Oriel and Barber method to obtain a third product and a second control for the Oriel and Barber material.

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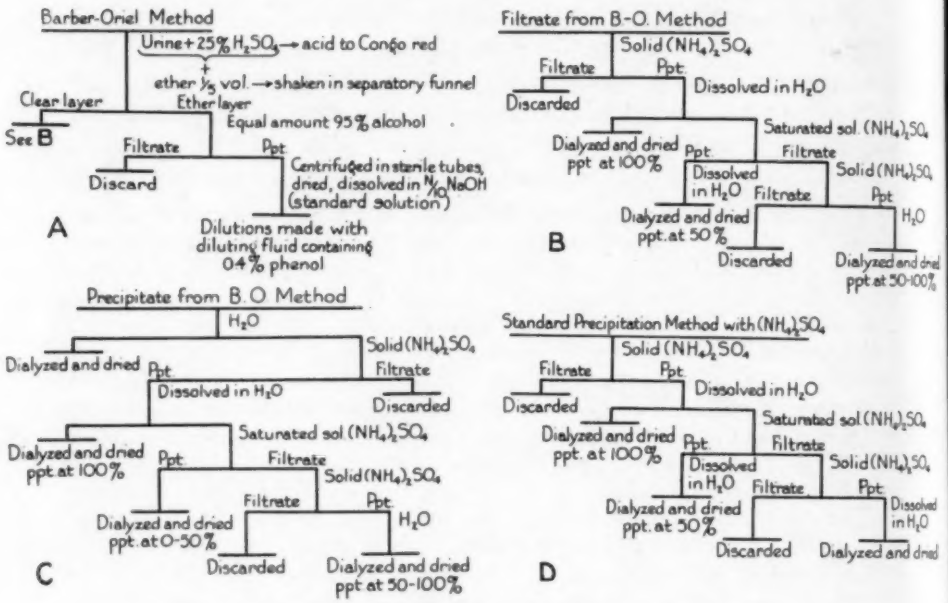
6. (*a*) Freeman, J.: Specificity of the Proteose Intradermal Reaction, Lancet **1**:561 (March 12) 1932. (*b*) Lyon, R. M.; Percival, J. H., and Stewart, C. P.: A Note on Urinary Protein, Brit. M. J. **1**:136 (Jan. 23) 1932. (*c*) Aldred-Brown, G. R. P., and Munro, J. M. H.: Autogenous Urinary Proteose in Rheumatoid Arthritis, Lancet **2**:1211 (Dec. 3) 1932. (*d*) Eichenlaub, F. J.: Proteose in Dermatoses, Arch. Dermat. & Syph. **27**:316 (Feb.) 1933. (*e*) Cormia, F. E.: Urinary Proteose, Arch. f. Dermat. u. Syph. **27**:745 (May) 1933. (*f*) Steel: Specificity of Proteose, M. J. Australia **2**:800 (Dec. 31) 1932. (*g*) Vaughan, W. T.: So-Called Urinary Proteose in Individuals Allergic to Ragweed, J. Allergy **4**:385 (July) 1933.

In the precipitation method the urine was filtered and saturated with solid ammonium sulphate (after experimenting with both hot and cold solutions of ammonium sulphate and seeing that similar precipitates were obtained, all further work was done using only the cold solution). The resulting precipitate was filtered off and dissolved in distilled water. One half of this solution was dialyzed and dried at room temperature. The other half was added to equal parts of saturated ammonium sulphate solution. The resulting precipitate was dialyzed and dried, the filtrate saturated with cold ammonium sulphate and the latter precipitated, dialyzed and dried.

We believed it would be an improvement on the Oriel and Barber method if the material was free from salts. We therefore dissolved the precipitate obtained from the ether extraction and alcohol precipitation in water. One half of this solu-



Methods used in obtaining proteose from urine.

tion was dialyzed against distilled water freed from salts and then dried. The other half was saturated with solid ammonium sulphate. The filtrate from this saturation was freed from sulphate by the barium carbonate method and was then tested for protein material by the biuret method; the result was negative. The precipitate obtained at 100 per cent saturation was dissolved in water. One half was dialyzed and dried; the other half was precipitated at 50 per cent and 100 per cent saturation. These precipitates were dissolved in water and dialyzed and dried. We wished to know if all the protein material is removed by the Oriel and Barber method, and to that end used the filtrate which they discarded to be worked through by the precipitation method as if it were the original urine. By doing this we obtained a material which was analogous both to the Oriel and Barber material and to that obtained by the precipitation method on the original urine. The materials obtained were the precipitates at 50 per cent, at from 50 to 100 per cent and at 100 per cent saturation with ammonium sulphate.

All the materials obtained by the various procedures were used for epidermal, intradermal and patch tests, and representative samples were used according to the method of Prausnitz and Küstner.[7] They were also used in attempts to immunize rabbits and as therapeutic agents.

Our work on the urine of patients with eczema was checked by similar procedures on urine from normal persons and from patients with Hodgkin's disease, carcinoma and tuberculosis, as well as from those with asthma, hay fever, urticaria and angioneurotic edema.

Physical and Chemical Properties of Proteose Substances Precipitated by Various Methods

	Substance							
	Barber-Oriel	Barber-Oriel after Dialysis	Barber-Oriel Precipitate at 50%	Barber-Oriel Precipitate at from 50 to 100%	Barber-Oriel Precipitate at 100%	Ammonium Sulphate Precipitate at 100%	Ammonium Sulphate Precipitate at 50%	Ammonium Sulphate Precipitate at from 50 to 100%
Solubilities								
H_2O*	+	+	+	+	+	+	+	+
10% sodium chloride	+	+	+	+	+	+	+	+
0.2% hydrochloric acid	+	+	+	+	+	+	+	+
0.5% sodium carbonate	+	+	+	+	+	+	+	+
Concentrated hydrochloric acid	+	+	+	+	+	+	+	+
Concentrated potassium hydroxide	+	+	+	+	+	+	+	+
Color Tests								
Millon's	±†	±	±	±	±	±	±	±
Xanthoproteic	+	+	+	+	+	+	+	+
Hopkins-Cole	±†	±	±	±	±	±	±	±
Biuret	+	+	+	+	+	+	+	+
Molisch	+	+	+	+	+	+	+	+
Precipitation Tests								
Nitric acid	—	—	—	—	—	—	—	—
Corrosive mercuric chloride	+	+	+	+	+	+	+	+
Potassium ferrocyanide, acetic acid	—	—	—	—	—	—	—	—
Potassium mercuric iodide	+	+	+	+	+	+	+	+
Alcohol	+	+	+	+	+	+	+	+
Trinitrophenol	+	+	+	+	+	+	+	+
Trichloracetic acid	—	—	—	—	—	—	—	—
Salts								
Ammonium sulphate	+	+	+	+	+	+	+	+
Sodium chloride	—	—	—	—	—	—	—	—
Dialysis	—	—	—	—	—	—	—	—
Coagulation	—	—	—	—	—	—	—	—

* Goes into solution easily when moist; after drying, only partially and with difficulty.
† Faintly positive.

In order to ascertain the irritability of the skin and whether the various test materials were nonspecific irritants, we checked all skin tests with physiologic solution of sodium chloride, water and solutions of salts in proportion to those commonly found in normal urine. We tested each person's reaction, not only to proteose from his own urine, but also to the proteoses obtained from others. Materials obtained at various saturations with ammonium sulphate were used for additional tests. Samples of all the material obtained were used for testing normal persons used as controls. To ascertain if the Oriel and Barber method

7. Prausnitz and Küstner: Studien über Ueberempfindlichkeit, Centralbl. f. Bakt. (Abt. 1) **86**:168, 1921.

specifically precipitates proteose alone, three different solutions, namely, one containing the salts usually found in normal urine, a 1 per cent solution of albumin and a 1 per cent solution of proteose-peptone were subjected to it. Similar precipitates were obtained in each case.

CHEMICAL FINDINGS

A white, powdery, amorphous material was obtained in every case except by the standard precipitation method, by which a material was obtained that was colored by the urinary pigment and had a gummier consistency. Proteose materials, whether obtained by the standard or by the Oriel and Barber method, and whether obtained from the urine of persons with allergic or from that of persons with nonallergic diseases, have the same chemical properties, as shown in the table. The standard method gave a material which was free from salts, whereas the material obtained by the Oriel and Barber method contained salts mixed with the proteose.

BIOLOGIC RESULTS

The various materials obtained by the several procedures were used to make epidermal, intradermal and patch tests. With each of them a localized erythematous reaction appeared at the site tested, the reaction coming on soon after the test was made and being more intense in areas affected by the dermatitis than in normal-appearing areas on the same persons. The erythema lasted from a half-hour to an hour, and in some cases was followed twenty-four hours later by faint erythema at the same site. The same reactions were obtained in some persons with 1 per cent solution of sodium chloride, and 1 per cent solutions of albumin and of proteose-peptone.

Therapeutically solutions were used subcutaneously for extended periods, following the procedure of Oriel and Barber, without noteworthy changes. The attempt at immunizing rabbits with the various materials obtained failed. The blood serum of these rabbits showed no precipitating powers against the solution of the urinary substances used in their attempted immunization. The Prausnitz-Küstner reactions were all negative.

COMMENT

The idea that the kidney might excrete substances formed from allergic reactions in tissues is not all fanciful. Thus, workers have found some evidence that certain organs, e. g., the liver, react with antigens to produce new substances such as the anaphylatoxins postulated by Friedberger. It is the consensus of modern students that any foreign protein in the blood stream will be excreted by the kidney. There is some evidence, too, that allergic processes produce split products from conjugated ones, which might then be small enough to go through the

kidney (Vaughan [8]). We do not feel, however, that an allergic person excretes a specific substance peculiar to himself. Our reasons for this opinion are that similar reactions can be obtained in patients with eczema when salts of the type and in proportions found in urine are used. Similar reactions are also found when material is used from normal urine and from solutions of proteose-peptone and of albumin. In addition, the attempt to immunize rabbits failed, and last, the skin tests on allergic persons with substances obtained from their own urine were negative. In many cases material obtained from a person's urine gave a weaker reaction when tested on him than when used on another.

On the other hand, several authors [9] have agreed with Oriel and Barber in their contention that the material obtained in allergic persons contains specific substances. They based their opinion on the fact that they obtained positive Prausnitz-Küstner reactions and secured negative reactions to proteose from other persons in patients who gave a definite reaction to proteose from their own urine.

We feel that such reactions as may be obtained in persons with eczema, at least, should be interpreted with the greatest caution. The areas in an inflammatory state require as little as the prick of a sharp needle to produce a local reaction. The normal-appearing skin in these persons is hyperirritable. One of us (T. C.) has found that the threshold of irritability near the margin of areas affected in some dermatoses is smaller the nearer the area is approached, which is some evidence that the apparently normal skin near a patch of dermatitis has been altered. We are therefore skeptical of the positive reactions obtained on the irritable skin of patients with eczema, particularly since the materials used contain salts and other irritants. At any rate, leaving aside the material used, we did not gain such positive reactions, in the sense of Lewis,[10] as the triple response, wheals with pseudopodia, blanching and erythema. The reactions that we saw were merely erythematous, with at most some edema.

The substances extracted from the urine of patients with eczema or from that of normal persons may produce an erythematous reaction even when injected into the skin of seemingly normal persons. If one assumes that the latter have indeed normal skins, one is forced to

8. Vaughan, V. C.: The Protein Poison in Its Relation to Disease, J. A. M. A. **61**:761 (Nov. 15) 1913.

9. Darley, W. D., and Whitehead, R. W.: Proteose from Allergic Patients: Skin Reactions and Therapeutic Applications, Colorado M. J. **28**:293 (July) 1931; Proc. Soc. Exper. Biol. & Med. **26**:688 1931; Skin Reactions and Therapeutic Applications in Hay Fever, Ann. Int. Med. **6**:389 (Sept.) 1932. Lyon, Percival and Stewart.[6b] Aldred-Brown and Munro.[6c]

10. Lewis, T.: Blood Vessels of the Human Skin and Their Responses, London, Shaw & Sons, Ltd., 1927.

conclude that the materials themselves have irritating properties for any skin. Otherwise, the normal controls were that in appearance only.

It might properly be objected that negative skin tests do not remove the possibility of a specificity of the test substance. With the shock tissue itself, however, being used as the test organ, as in eczema, one would have more reason to believe that the specific antigenic substance should excite a positive reaction, particularly when it is used in a patch test. If it does not, and we found it not to, one would be inclined to think that the test material is not a specific antigen. If it is neither an antigen nor a derivative of an antigen, it must be a substance elaborated by metabolic processes unrelated or incidental to allergic phenomena. It may be a by-product of an allergic process. What seems to give foundation to this is the fact that urine of allergic persons yields larger quantities of precipitate. On the other hand, we were forced to conclude that normal-appearing persons have allergic processes, not appreciable on inspection, since their urine likewise produces a substance in every way comparable to that found in the urine of allergic persons. The fact that a larger quantity of the substance appears in the urine of allergic persons, as compared with that of normal persons, does not seem to us to prove necessarily that it is involved in the process specifically. It is just as easy to uphold the thesis that the production of such material is simply incidental to all allergic processes.

We subjected the products prepared by the Oriel and Barber method to dialysis. As a result of the use of the dialyzed material we believe that salts were responsible in part for any skin reactions which Oriel and Barber obtained, because our products produced much smaller reactions, if any, when freed from salts by dialysis. While it may be argued that certain proteoses are dialyzable, the substances we obtained, other than salts, were not able to pass the collodion membranes. The nondialyzable substances gained immediate negative skin reactions and a few delayed erythematous ones. Normal and allergic urines yield their substances at the same degree of fractionation, which seems to be further evidence that the substances obtained in different urines are not specific and variable. It is possible that this substance is indeed common to all allergic persons, but requires to be conjugated with a specific substance in each case. Thus, the specific reacting substance from the pneumococcus has been found not to be a protein or protein in nature, but a carbohydrate, which requires linkage to a protein to be provided with antigenic powers. The work of Landsteiner and Lampl [11] showing that a simple dye substance may act as the specific radical when attached to a

11. Landsteiner, K., and Lampl, H.: Ueber die Abhängigkeit der serologischen Spezifizität von der chemischen Struktur: VII. Mitteilung über Antigene, Biochem. Ztschr. **86**:343, 1918.

nonspecific protein supports this view. One is not surprised to obtain positive pseudoreactions in eczematous persons as well as in normal persons with the Barber-Oriel substances, in view of the demonstration by Koessler [12] and by Huber of a histamine-like substance in the blood of allergic persons. The traumatization of skin resulting from the use of the needle and urinary salts will produce in themselves histamine-like substances (Lewis [10]). When this is added to subthreshold quantities already present in a skin with potentiality for easy irritation because of near or distant inflammation, threshold quantities for reaction can easily be conceived to follow.

The failure to immunize rabbits might have been anticipated in view of the work of Funk,[13] Landsteiner [14] and others, who showed that it was impossible to immunize animals when proteose solutions were used for antigens, in contrast to proteins of larger molecular size.

If one studies the table of the physical and chemical properties of these various substances, it will be noted that it matters little which method is used for obtaining them. They all have the same chemical properties. We take exception to the Barber and Oriel method because it does not remove all the proteose from the urine and, furthermore, yields an impure substance, a mixture of the proteose substance with salts and organic materials. The standard precipitation method gives a purer substance and a more complete separation of the proteose. The only possible objection is that the urinary pigments are precipitated to some extent by the latter method.

As far as the proteose is concerned, we find that this can be obtained from all urine, from that of normal persons or others; it gives a positive Molisch reaction as well as a positive reaction to the protein color tests. It is not coagulable by heat, and is precipitated in the cold by ammonium sulphate. It therefore belongs to the conjugated or derived protein group, and is probably a proteose or, because of the positive Molisch reaction, a glycoproteose. This material is possibly found in the urine because it occurs as one of the proteins during the stage of digestion and, because of its small molecular weight, is excreted in various amounts through the normal kidney.

SUMMARY

The work of Oriel and Barber has been repeated in fourteen patients with eczema, ten persons with nonallergic conditions and five normal persons. The standard precipitation method in general use by bio-

12. Koessler, K. K.; Lewis, J. H., and Walker, J. A.: Pharmacodynamic Actions of Bacterial Poisons, Arch. Int. Med. **39**:188 (Feb.) 1927.

13. Funk, E. B.: Antigenic Properties of Proteose, J. Infect. Dis. **25**:97, 1919.

14. Landsteiner, K.: Experiments on Anaphylaxis to Azoproteins, J. Exper. Med. **39**:631, 1924.

chemists and the Barber and Oriel technic were used parallel. The materials obtained were used for various skin tests, in attempts to immunize rabbits and therapeutically.

CONCLUSIONS

1. Similar proteose-like substances are obtained by the Barber and Oriel technic and the standard method of precipitation with ammonium sulphate.

2. The materials obtained from the urine of allergic patients, persons with nonallergic diseases and from normal persons cannot be distinguished from one another by the various tests we applied.

3. Epidermal and intracutaneous tests in allergic patients with the proteose-like substances give only pseudoreactions.

4. Patch tests and Prausnitz-Küstner reactions to proteose-like substances are negative.

5. These substances are not antigenic.

6. As therapeutic agents they are ineffectual.

ABSTRACT OF DISCUSSION

Dr. Robert E. Barney, Cleveland: Oriel and Barber, in their original communications, expressed the belief that the urinary proteoses excreted by patients suffering from allergic disorders contain specific antigens. By using these proteoses therapeutically, favorable results were recorded. Subsequent investigations by other authors as a rule yielded results far from encouraging.

The careful work of Dr. Cornbleet and Dr. Kaplan failed to demonstrate specific antigens in the urinary proteoses of patients with allergic eczema, and their therapeutic attempts were without result, in spite of the fact that they used purer substances.

Oriel and Barber may have been fortunate in collecting the urine of allergic subjects at a time when it contained large amounts of antigen, hence their favorable therapeutic results; or the proteoses, acting similarly to foreign proteins, may have been in part responsible.

Even though the therapeutic results thus far have been discouraging, any method which may prove beneficial in the treatment of so-called allergic eczema merits further investigation.

Dr. Frank J. Eichenlaub, Washington, D. C.: This paper demonstrates conclusively that by the method of Barber and Oriel no specific antigen can be obtained. The investigation by Dr. Cornbleet and Dr. Kaplan is considerably more complete from the laboratory standpoint than my own, and I must say that a number of the patients in whom I reported favorable results have since had relapses and have failed to respond to further treatment.

On the other hand, there have been enough (a very few, but enough) outstanding therapeutic results from the method of Barber and Oriel to make me feel that the method should not be abandoned without further consideration. Even if it is only seldom that a stubborn eczema is improved and only occasionally that one is cured by this method of injection, I think it is worth a trial. Even if

work should show that the specific antigen is picked up only occasionally, or even if the therapeutic results are obtained because of a nonspecific action, or because of some chemical substance present, I think that the method should not be abandoned until every one is sure that it will not do some good.

Dr. Max E. Obermayer, Chicago: At the University of Chicago my colleagues and I have followed the problem of the urinary proteose with interest and have experimented in a number of cases of neurodermatitis and dermatitis herpetiformis. We have followed the technic of Oriel and Barber closely in preparing the proteose and administering the injections. A positive reaction was invariably obtained, which consisted of erythema and a central papule or nodule. Its intensity varied with the amount of proteose injected and the sensitivity of the skin of the individual patient. It was by no means specific. The intensity was about the same whether the patient's own proteose was given or that of another patient.

Normal controls did not react differently from the patients.

Proteose when injected intradermally seems to have no specific effects. The proteose obtained by the Barber and Oriel method has nothing to do with the allergic mechanism, but seems to act as a local irritant only.

Our experiences with proteose are thus the same as those of Cornbleet and Kaplan, and I congratulate them on the excellent chemical work which they have done.

Dr. Warren T. Vaughan, Richmond, Va.: The search for some nonspecific cure-all in allergy will continue and should continue, and it is hoped that something will eventually be discovered. When the work of Oriel and Barber was first reported, I tried the method, got nowhere, discarded it, and then, with the appearance of several enthusiastic articles, I considered it possible that I had made a mistake. I felt that if one actually knew what was causing the patient's symptoms and tried to find that substance or some related substance in the urine, one would be in a better position to judge the value of the method. I took patients with ragweed hay fever, and attempted to obtain from their urine during the attack of hay fever something that could be associated with the cause of their trouble. The specimens of urine, when tested in the patients and in other persons sensitive to ragweed gave no positive reactions. Passive transfer or the Prausnitz-Küstner antibody could not be demonstrated. I obtained no improvement in the hay fever or in the ragweed asthma following treatment with the proteose.

I think that new preparations which are offered as yielding specific desensitization and nonspecific substances which reduce the allergic response should be investigated and reports made, as has been done this morning. I have tried out intravenous injections of nitrohydrochloric acid, and the rest, as they came along. Unfortunately, up to the present I must continue with specific allergic therapy.

Dr. Theodore Cornbleet, Chicago: I do not feel that this subject has been entirely closed, for positive results always take precedence over negative ones. It is just possible that we missed the antigenic material in our attempts to isolate it, which, I think, would certainly be a coincidence. On the other hand, it might be that by further work or variation of the method some positive results could be obtained.

I think, however, that instead of the proteose which is gotten laboriously from the patient's own urine and is, so far as any one yet knows, nonspecific, one can just as well substitute peptone, a material which can be obtained easily and in a relatively pure form.

IODIDE THERAPY FOR RELIEF OF PAIN IN AINHUM

REPORT OF A CASE

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Ainhum, a tropical disease seen mainly in Negroes, is on rare occasions observed in temperate climates. In some cases little or no pain is experienced, but the majority of reports in the literature indicate that pain is a cardinal symptom. It is evident that in the terminal phase, when the involved area becomes gangrenous and spontaneous amputation is about to result, subjective symptoms may disappear. Early in the disease, when there is little constriction, there is little discomfort, but as the process advances and the ever-tightening band interferes with the nerve and blood supply to the distal part of the toe, pain sets in. A case of this nature, in which the pain was relieved by iodide therapy, is herewith reported.

REPORT OF A CASE

A Negro, aged 41, a laundry worker, was born in Trinidad, British West Indies. He migrated to New York ten years previous to this report, and from that time resided there, at no time visiting a foreign country. In June 1933 he accidentally struck the toes of the left foot. There were slight tenderness and discomfort for a few days. No abnormality of the little toe was detected. In December, because of pains which gradually increased in intensity, the patient's attention was again directed toward the left fifth toe. The area was tender and painful, both when the patient was walking and when he was at rest; in fact, this symptom became so severe as to disturb his sleep. A change in the color and contour of the affected toe was visible at this time. In February 1934 the pain was just as severe, but was experienced only when the patient was walking; there was no discomfort while the foot was at rest. It was because of this disability that the patient sought relief at the dermatologic clinic of Harlem Hospital. He had received various types of medication without relief. There was no history of a similar disease in the family. The Wassermann reaction of the blood was doubtful. There was no clinical history of syphilis.

The distal half of the left fifth toe was circular, flat and purplish. The firm, hard constricting ring was limited to the plantar surface and was situated ¾ inch (2 cm.) above the base of the toe. The dorsalis pedis artery was pulsating normally.

From the Department of Dermatology and Syphilis, Harlem Hospital.

Sodium iodide solution (31 grains [2.008 Gm.]) was injected intravenously. About six hours later the patient felt decided relief, and shortly afterward the pain disappeared completely, so that he was able to walk without discomfort. When he was seen after the intravenous injection, he stated he felt a constricting, suffocating sensation in the sternal area, with dizziness and pains in the head. Because of this, the intravenous injections were not continued, and oral administration of potassium iodide (10 grains [0.65 Gm.]) three times daily was substituted, but this also had to be discontinued. Within two weeks the affected toe became dark purple, and the lesion was painless. The patient failed to return to the clinic for further observation.

A review of the current literature does not reveal the use of iodides in this disease. If it is possible to relieve pain in ainhum by the intravenous injection of sodium iodide, something worth while has been accomplished in alleviating the suffering of those who refuse to submit to surgical measures.

SUMMARY

A case of ainhum in which severe pain of about ten weeks' duration was the chief complaint is presented. A few hours after a single intravenous injection of 31 grains of sodium iodide, this symptom disappeared; it had not returned fourteen days later, when the patient was last seen.

It is advisable to give this type of therapy a thorough trial in patients who complain of severe pain and who refuse to permit surgical intervention.

ULCUS VULVAE ACUTUM ACCOMPANIED BY DISEASE OF SKIN AND OF ORAL MUCOSA

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Ulcus vulvae acutum, originally described by Lipschütz,[1] was considered by him to be a local infection with Bacillus crassus. Recently, Samek and Fischer,[2] in a patient aged 19 who had ulcers within the vulva and an erythema nodosum-like eruption on the legs, demonstrated B. crassus bacteriologically, in cultures from the surface of ulcers and skin nodes and from the blood, and in histologic sections. Their interpretation was that of a general B. crassus infection with metastases to the skin.

Later Ito, Matras [3] and Philadelphy [4] obtained B. crassus both in smears and in culture from aphtha-like lesions on the mucosa of the mouth, concurrent with typical genital ulcers.

Thus, not only can B. crassus cause local ulcerations of the external genitalia, but the organism may be responsible for generalized infection, as is borne out by the first case to be reported here.

REPORT OF CASES

CASE 1.—In a school girl of 16 years there appeared suddenly a pustular eruption on the face, accompanied by a chill and fever (temperature 39 C, 102.2 F.). That evening the patient noticed an ulcer on the left labium majus, and in the course of the next few days the eruption spread to the scalp and trunk. Simultaneously numerous painful ulcers appeared in the region of the vulva.

The patient had had measles, mumps, inflammation of the lungs and tuberculosis of the lymphatic glands. The menses began at the age of 15; they were irregular, appearing every two or three months; they were of five days' duration, not copious and painless. Slight nasal hemorrhages occurred periodically. The patient was of middle height and regular build. Secondary sexual signs were expressed weakly. A moderately enlarged thyroid gland was palpable. The neck and the submaxillary lymphatic glands were markedly enlarged and compressed tightly. There were increased breath sounds in the apex of the right lung.

On the scalp, face, trunk and right upper extremity there were numerous pustules varying in size from that of a pinhead to that of a small pea, surrounded

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From the dermatological clinic of the Perm Medical Institute and of the Perm Branch of the Ural Province Venereological Institute, headed by Prof. M. A. Rosentoul.

1. Lipschütz, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 21.

2. Samek, J., and Fischer, E.: Arch. f. Dermat. u. Syph. **158**:729, 1929.

3. Matras, A.: Arch. f. Dermat. u. Syph. **166**:491, 1932.

4. Philadelphy, A.: Dermat. Wchnschr. **46**:1052, 1933.

by a bright hyperemic halo. Some of them were arranged in nodose formations, varying in size from that of a hemp grain to that of a lentil. In the right axilla there were two fairly deep, pea-sized, oval ulcers. The borders of the ulcers were raised, hyperemic and slightly undermined. The base of each ulcer was covered with a fibrinopurulent coating.

The genitalia were those of a virgin. On the right labium majus and the left labium minus, in the inguinal creases, on the perineum and around the anus there were numerous ulcers of different sizes and shapes with slightly raised, undermined rims, covered with a grayish-yellow fibrinous coating, extremely painful to touch. The vaginal secretions were scanty, liquid, grayish and of acid reaction.

In the mouth, in the region of the left wisdom teeth as well as on the gums around the upper and lower incisor and canine teeth there were numerous small superficial ulcers of different sizes and shapes, covered with a moist grayish-white coating, surrounded by a bright hyperemic halo. Besides the ulcers there were ruby patches the size of a hemp grain. The gums were slightly inflamed; the pharyngeal mucosa was hyperemic, and the tonsils were enlarged.

In the secretion from the ulcers of the vulva were a great many B. crassus, leukocytes and a few gram-positive cocci and pseudodiphtheria bacteria. In the secretions from the ulcers of the mouth and the axilla single specimens of the type of B. crassus were found besides cocci. The pustular matter was sterile. The Wassermann, Sachs-Georgi and Kahn reactions were negative; the Pirquet reaction was positive. Auto-inoculation gave negative results.

With indifferent local therapy the ulcers cicatrized in twelve days. An ulcer from the right armpit was excised for biopsy.

The epidermis around the ulcer showed moderate acanthosis. Interpapillary continuations of epidermis having the shape of massive, tonguelike protrusions were embedded in the derma. In the rete Malpighii the intercellular interstices were widened, with single leukocytes in the lumens. The area of epidermis adjacent to the rim of the ulcer was becoming thin and gradually passed into the ulcer surface. Spongiosis and invasions of leukocytes were most pronounced here.

In the derma on the circumference of the ulcer in the areas covered with epithelium the papillary layer was edematous, the capillaries were enlarged, their endothelium was swollen, and a meager infiltration of leukocytes, fibroblasts and single leukocytes surrounded them.

Enlarged lumens of the blood, and in the upper layers also of the lymphatic, vessels were seen along the whole length of the preparation and penetrated into the subcutaneous fat cells. In the edematous tissue surrounding the vessels was an insignificant infiltrate of lymphocytes, fibroblasts and single plasma cells.

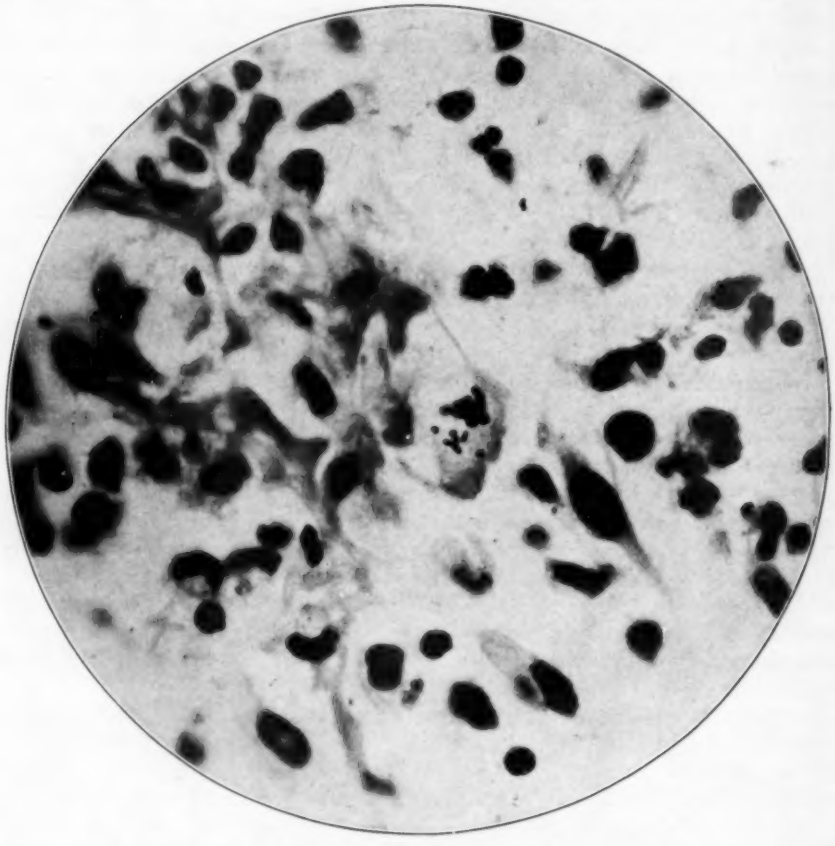
On the surface of the ulcer a narrow strip of suppurating fibrinous coating was to be seen. Below it, in the papillary and subpapillary layers, the collagenous tissue was markedly edematous and was pervaded by a rather thick infiltrate. There were numerous blood vessels extending in all directions, enlarged and filled with erythrocytes and leukocytes. In places in the infiltrates not many erythrocytes were seen.

In the middle and deep layers of the derma foci of infiltration were observed around the enlarged blood vessels.

In the subcutis the infiltrate was distributed diffusely, replacing the fatty tissue in part. Changes in the vessels were chiefly observed in the upper layers of the infiltrate.

The vascular walls were thickened, edematous and pervaded here and there by fairly numerous leukocytes. Among the leukocytes were swollen connective tissue

cells of the intima with oblong to oval, pale nuclei. The vessel endothelium was swollen. In the deeper layers of the derma the edema of the vascular walls was less pronounced. Among the cells of the infiltrate, lymphocytes, histiocytes and fibroblasts prevailed. Leukocytes and single plasma cells occurred more rarely. At the periphery of the infiltrate, on the boundary from the sound tissue, there occurred accumulations of strongly dyed nuclei of different shapes. In form some were like coarse, long rods with broken ends, some like threads stretched out and others hooked.



Section from the middle layer of the derma (case 1), showing thick rods glued together and single ones of the type of B. crassus.

The elastic tissue was absent or in shreds in the region of the infiltrate; outside the infiltrate it exhibited no changes. The sweat and apocrine glands and the hairy follicles occurring in the preparations were not changed, except that the infiltrates around the vessels permeated the region of the tubercles of sweat glands.

In one of the numerous preparations within the middle layers of the derma amid the infiltrate were observed thick rods glued together and single ones of the type of B. crassus, as shown in the accompanying illustration.

Comment.—The character of the histologic changes, the presence of B. crassus in the smears from the surface of the ulcers and in histologic sections and the general course of the disease indicate that in this case there was a general B. crassus infection. An extremely poor content of B. crassus in the sections from the ulcer was also noted. Apparently the condition must be considered as a manifestation of allergy by analogy with other infections. Positive cutaneous reactions obtained by Rosenthal [5] indicate the possibility of the development of allergic reactions.

If in this case, as well as in the observations of Samek and Fischer, Ito, Matras and Philadelphy, the clinical phenomena are explained by the general B. crassus infection with metastases to the skin and mucous membranes, somewhat different relations exist in a number of other cases with an analogous clinical course as in case 2.

Case 2.—A woman, aged 28, had been suffering for one and one-half years from aphthous stomatitis and ulcers on the genitalia. The aphthae appeared in the mouth one and one-half years before the patient was seen, and three weeks after their appearance there arose painful ulcers on the right labium minus and left labium majus.

In spite of treatment, the lesions in the mouth had been recurring ever since; the ulcer on the left labium majus had been constantly present for one and one-half years. Four more ulcers had appeared in the region of the vulva during the last menses. The ulcers were so painful that the patient was forced to retire and become a pensioner.

She had been married for six years. She had had no pregnancies or diseases. She denied having any pathologic heredity. She was of middle height and normal build. On the skin of the trunk there were scattered acne lesions; on the shins and thighs there was lichen pilaris. In the mouth, on the mucosa of the upper and lower lips, there were typical aphthae in different stages of development.

The left labium majus and the labia minora were edematous. In the lower third of the left labium majus a deep ulcer of irregular, oval shape, the size of a penny, was forming. The base of the ulcer was indurated; the rim was raised in places and slightly undermined. The bottom of the ulcer was covered with a grayish-yellow fibrinous coating. Ulcers of various sizes and shapes occupied the sites of the lower wall of the vagina, the posterior commissure and the left labium majus. The rims of the ulcers were in places raised, cylinder-like, hyperemic and slightly undermined. The bottoms were covered with a grayish-yellow fibrinous coating.

The inguinal and submaxillary lymphatic glands were somewhat enlarged and slightly painful. The inner organs were normal. The Wassermann, Sachs-Georgi and Kahn reactions were negative.

The smears from the ulcers on the genitalia abounded in B. crassus and sometimes contained gram-positive cocci. In the preparations of the ulcers of the oral mucosa there was a varied flora.

The culture mediums for the secretions from the genital and oral ulcers were agar, ascites-agar and sugar-agar; the medium for the blood was sugar solution. The cultures from the ulcers of the mouth furthered the growth of staphylococci

5. Rosenthal, S. K.: Arch. f. Dermat. u. Syph. **162**:95, 1930.

and streptococci. The blood cultures were sterile. The cultures from the genital ulcers gave rise to numerous colonies of staphylococci around which there were established typical feltlike colonies of B. crassus; this was verified bacterioscopically. An ulcer from the right labium majus was removed for biopsy.

As a result of treatment with neoarsphenamine lotion the genital ulcers cicatrized in one and one-half months, whereas the aphthae in the mouth continued to recur.

At biopsy the ulcer from the right labium majus was examined microscopically in toto. The bottom of the ulcer was nearly on the level of the epidermis. On the portions of the epidermis adjacent to the surface of the ulcer the cells of the horny and basal layers almost did not become colored and in places kept the remnants of nuclei. The borderline between the epidermis and dermis was smooth. The granular layer was not pronounced. The corneous layer, changed parakeratotically, was densely pervaded by leukocytes. In the regions lying remote from the ulcer the epidermis was in a state of acanthosis, with symptoms of spongiosis not sharply expressed. The papillary and subpapillary layers were edematous, with a considerable accumulation of leukocytes. The blood vessels were enlarged, and the endothelium was swollen. On the surface of the ulcer there was a salient narrow strip of leukocytes, erythrocytes and fibrinous masses. Below it the upper layers of the derma were markedly edematous, and the blood vessels were enlarged. In the copious infiltrate consisting chiefly of leukocytes and lymphocytes there were narrow connective tissue layers, which had in part kept their elastic fibers. This zone of the infiltrate in places extended tonguelike into the middle layers of the derma. In numerous enlarged blood vessels there were accumulations of leukocytes. The vascular wall was edematous, pervaded by emigrant leukocytes. In the middle layers of the derma the most marked changes in the vessels were observed. The lumens of the vessels were enlarged and contained leukocytes. The vascular walls were edematous and defibrillated. The endothelium was swollen, in part penetrating into the lumens of the vessels. There was a considerable proliferation of adventitial cells, among which were seen numerous emigrant leukocytes, often having rather peculiar forms of nuclei. At the periphery the vessels were surrounded by a fairly mighty rampart of infiltrate, consisting mainly of young connective tissue cells and lymphocytes.

These connective tissue cells seemed to be differentiated, and part of them were possibly degenerate adventitial cells of the vessels. They had a peculiar structure, some being long rods, some hooklike, some macelike and some spindlelike, with long protoplasma fibers. They were located in connection with vessels, mainly in the middle and deep layers of the derma, though single heaps occurred also in the superficial infiltrate, at first glance resembling accumulated bacteria in the shape and the intensity of coloration.

I must call especial attention to the foci of infiltration with analogous changes in the vascular walls remote from the fundamental focus.

Among the infiltrate cells there occurred, besides leukocytes, lymphocytes and fibroblasts, histiocytes and single plasma and fat cells. In the region of the infiltrate there occurred only scraps of collagenous and elastic fibers. The sebaceous hair follicles and sweat glands were not changed.

Bacteria were absent both on the surface of the ulcer and within the tissues.

Comment.—In this case, a married woman, aged 28, presented aphthous stomatitis and in connection with the menses ulcers on the

genitalia; the secretion of these ulcers contained B. crassus as was revealed both in smears and in cultures.

The histologic picture, with particular changes in the walls of the vessels, chiefly the veins, essentially corresponds to the changes which were described by Lipschütz [6] and Brünauer, Roederer and Sloimovici [7] as "ulcus vulvae acutum."

Protracted existence of some ulcers for one and one-half years is uncommon. I know of only one analogous case, demonstrated by Schwarzkopf [8] at the meeting of the Berlin Dermatological Society in 1930. A woman, aged 39, had changeless ulcus vulvae acutum for two years. The course of the disease indicates, in contrast to my cases, that ulcus vulvae acutum and aphthae are to be considered as two independent diseases. However, the observations of a number of authors (Lipschütz, Carol and Ruys,[9] Kumer,[10] Walter and Roman,[11] Levin [12] and others) allow of the assumption that the simultaneous existence of ulcus vulvae acutum and aphthae is not rare and hardly casual, as Lipschütz maintained.

The accumulation and study of similar materials will permit future investigators to approach nearer the solution of the problem of the relation between ulcus vulvae acutum and aphthosis.

SUMMARY

Two rare cases of ulcus vulvae acutum associated with lesions on the skin and mucous membrane of the mouth are reported. In the first case, a girl aged 16 suddenly had a chill, fever, pustular and papulopustular lesions on the skin, numerous ulcers typical of ulcus vulvae acutum on the genitalia and perineum, around the anus, in the inguinal creases and in the right axilla, and aphtha-like lesions on the mucosa of the mouth.

The smears from the ulcers on the genitalia, in the armpit and in the oral mucosa, as well as the histologic sections of the ulcers from the armpit, showed B. crassus.

In the second case, a married woman aged 28 had aphthous stomatitis and, in connection with the menses, extremely painful ulcers on the genitalia, one of which persisted for one and one-half years.

6. Lipschütz: Arch. f. Dermat. u. Syph. **136**:428, 1921.
7. Roederer, J., and Sloimovici, A.: Ann. de dermat. et syph. **9**:106, 1928.
8. Schwarzkopf: Dermat. Wchnschr. **92**:700, 1931.
9. Carol and Ruys: Acta dermat.-venereol. **9**:123, 1928.
10. Kumer, L.: Dermat. Ztschr. **57**:401, 1930.
11. Walter, F., and Roman, I.: Dermat. Wchnschr. **90**:705, 1930.
12. Levin: Hazanskiy med. j., 1931, no. 1.

The histologic investigation in the two cases revealed essentially similar pictures both in the ulcers of the armpit and in those of the genitalia.

In both cases the changes were revealed chiefly in the region of blood vessels, around which the infiltrate was concentrated.

In the first case the clinical symptoms were caused by the general B. crassus infection, with metastases to the skin and mucous membranes; in the second, ulcus vulvae acutum was accompanied by aphthosis.

DERMATITIS PRODUCED BY HYMOLAL SALTS

(A NEW SOAPLIKE MATERIAL)

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There has been a recent tendency to develop soaplike materials for shampoos; one of these is a solution of hymolal salts. This is a combination of sulphonated alcohols of high molecular weight combined with an alkali to form the neutral salt.

I have been unable to find reports in the literature of cases of dermatitis produced by the use of these new compounds.

REPORT OF A CASE

A white man, aged 35, a local "beautician," first consulted me in the middle of March for dermatitis of both hands. The irritation commenced about a week previously and gradually increased in severity. The history revealed the fact that about March 1 the patient commenced to use hymolal salts as a shampoo, giving an average of ten treatments a day.

Examination disclosed what first appeared to be a severe case of "chapped" hands. The skin was dry and erythematous, and the normal linear markings were greatly exaggerated. Over the knuckles were many small deep radiating fissures, and on the backs and palmar surfaces, thin scales the size of a dime could be removed. The patient complained of continual smarting. With the use of soothing therapy the hands were restored to their normal condition in ten days.

The patient returned to his work, and for another week no further trouble was experienced. Then, on resuming the use of the hymolal salts for shampoos his hands became red and immediately commenced to smart. The condition progressed until he discontinued the use of the shampoo and resumed the former treatment. At his last visit he reported that his hands remain well unless he uses the hymolal salts, which he has to do from time to time at the request of a client.

A comparative patch test was made on the forearm of the patient, using a solution of hymolal salts and a solution of the soap he generally used for a shampoo. After forty-eight hours the patches were removed; the erythema produced by the solution of hymolal salts was more pronounced. At the end of a week the site was observed again, and the area of skin which had been in contact with the new soaplike material had assumed the same characteristic skin changes as the hands: large, thin, exfoliating scales on an erythematous base with exaggeration of the normal lines of the skin. On the other hand, the solution of ordinary soap left no evidence on the skin of prior contact.

Summit Medical Group.

TUBERCULOID REACTION IN LYMPH NODES

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Diseases of the lymph nodes constitute an important phase of pathology, but despite careful study many of the reactions of lymphoid tissue are little understood.

In 1928, Michelson [1] reported an investigation of the inguinal nodes in early syphilis in which he found microscopically two different types of reaction to the infection: banal or nonspecific inflammation and the tuberculoid type of reaction characterized by epithelioid and giant cells without necrosis. The latter structure was observed in the nodes of 8 of 29 patients with early untreated syphilis. The work was continued, and a second report [2] was made in 1932, in which the histologic examinations of 145 lymph nodes from patients with early syphilis were reported, tuberculoid structure being found in 27 per cent of the cases.

It was believed that further study of this type might possibly throw some light on immunity in syphilis. This investigation was made in order to continue observation of the tuberculoid reaction in the nodes in early syphilis, to ascertain its frequency in nodes other than those of syphilitic patients and to determine, if possible, its significance.

NORMAL ANATOMY OF THE LYMPH NODES

The lymph nodes are structures which develop along the course of lymph vessels sometime during the third month of fetal life. They first appear in the axillary, inguinal and cervical regions where the lymphatics form a dense network in the meshes of which are masses of mesenchymal tissue which gradually become more and more cellular and with the surrounding vessels form the anlagen of the lymph nodes. These cells, which are lymphocytes, may, according to Bailey and Miller,[3]

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1. Michelson, H. E.: The Occurrence of Tuberculoid Reactions in the Inguinal Glands of Early Syphilis, Arch. Dermat. & Syph. **19**:66 (Jan.) 1929.

2. Michelson, H. E.: The Superficial Lymph Glands in Early Syphilis, Arch. Dermat. & Syph. **25**:457 (March) 1932.

3. Bailey, F. R., and Miller, A. M.: Text Book of Embryology, ed. 4, New York, William Wood & Company, 1931, p. 249.

pass through the walls of the vessels into the adjacent tissue or originate directly from the mesenchymal cells *in situ*. Whatever their origin may be, the cells divide freely, and the masses which they make up enlarge at the expense of the surrounding lymph vessels. Blood vessels which are destined to become the vascular supply of the node are present in the masses from the beginning. Many points concerning the origin and growth of the lymphatic system are still controversial. Most investigators agree that after its primary differentiation from the mesenchyme, the exact time and place of which is unknown, lymphatic endothelium becomes a specific independent tissue from which all of the lymphatics are developed. After the nodes have first appeared in the places occupied by the early lymphatic plexuses, the surrounding mesenchyme gives rise to the connective tissue elements: the capsule, trabeculae and reticulum. Jordan and Kindred [4] stated that the sinuses first appear as a result of differences in the hydrostatic pressure within the node, owing to the rapid proliferation of the lymphocytes in the formation of the nodules.

In the adult, lymph nodes appear in many areas of the body either singly or in large groups. They may vary in size from 1 to 25 mm. and are round, oval or reniform, depending on their relation to the surrounding structures. The surface is usually somewhat rough, and the color of the nodes depends on their position and function. Along the respiratory tract they may be black, owing to ingested pigment, while the mesenteric glands may be milk-white during digestion. Other nodes vary from pale pink to red. On one surface of each node there is an indentation or hilus, where the vessels enter and leave the structure.

The fully developed lymph node is made up of a supporting structure of connective tissue, lymphoid elements and lymph and blood vessels. It is enclosed in a fibrous capsule of closely packed bundles of collagenous fibers, a few fibroblasts and networks of thin elastic fibers. There are also a few smooth muscle cells at the points of entrance and exit of the lymph vessels. The capsule gives rise to projections of dense connective tissue, the trabeculae, which pass into and subdivide the node.

Throughout the node there are branching, anastomosing fibers which penetrate to all of its parts and form a framework which varies in density in different locations. This framework is connective tissue and is partially made up of the so-called argyrophil fibers, which are visualized by silver nitrate impregnation. The argyrophil fibers, which are also known as lattice fibrils, precollagenous fibers or *Gitterfasern*, originate from cells which arise from the mesenchyme and differ from elastic and collagenous fibers. Opinion is divided as to whether this difference

4. Jordan, H. E., and Kindred, J. E.: Embryology, New York, D. Appleton and Company, 1926, p. 176.

is chemical or physical. Rössle and Yoshida,[5] who extensively studied lattice fibrils in lymph nodes, stated that they were the forerunners of collagenous connective tissue, and that in certain areas they were found to be directly continuous with the collagenous fibers of the capsule and trabeculae.

The framework of the node also has a cellular syncytium which stands in intimate association with the fibers described in the preceding paragraph. These two elements (the cells and the fibers) have been loosely termed reticulum, but to avoid confusion it should be specifically stated whether one means reticular cells or fibers. The reticular cells or *Gitterfasern*-forming cells, according to Rössle and Yoshida, become flattened to form the so-called endothelial cells lining the lymph sinuses, which resemble true endothelial cells only in their appearance. Maximow [6] stated that they have the same properties of phagocytosing and storing as other reticular cells which are lacking in true endothelium. In recent years certain cells and groups of cells of mesenchymal origin which are similar in function have been classified together as the reticuloendothelial system. This includes the reticular cells of the lymph nodes, spleen, liver (Kupffer cells), suprarenal glands, bone marrow and hypophysis, the free connective tissue histiocytes, the blood histiocytes (dye-storing monocytes) and possibly the lattice fibrils of the corium and the dendritic cells of the epidermis. The other mesenchymal elements, the fibroblasts and the true endothelium of the blood and lymph vessels, having little or no phagocytic and storage properties, are thus functionally different and cannot be included in this system. The known facts, as well as the theories on this subject, have been recently discussed in a thorough manner by Schreiner and Wendleberger.[7]

The lymphoid portions of the node are arranged peripherally in follicles separated by the trabeculae to form the cortex and centrally as cords and more or less compact areas of lymphocytes constituting the medulla. The follicles, which consist of densely packed masses of lymphocytes, with occasional plasma cells and eosinophils, are also known as the primary nodules. Many contain pale, round centers, which are the secondary nodules or germ centers, the size and number of which vary considerably. Flemming [8] maintained that they represent the point

5. Rössle, R., and Yoshida, T.: Das Gitterfaserngerüst der Lymphdrüsen unter normalen und pathologischen Verhältnissen, Beitr. z. path. Anat. u. z. allg. Path. **45**:110, 1909.

6. Maximow, A.: A Text Book of Histology, Philadelphia, W. B Saunders Company, 1930, p. 375.

7. Schreiner, K., and Wendleberger, J.: Ueber das reticulo-endotheliale System, Zentralbl. f. Haut- u. Geschlechtskr. **47**:369, 1934.

8. Flemming, quoted by Zurhelle, E.: Die Syphilis der Lymphgefässe und Lymphdrüsen, in Jadassohn, J.: Handbuch der Haut und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 17, pt. 3, p. 1.

of formation of the lymphocytes. The medullary substance is cytologically identical with the cortex, but owing to the loose arrangement of the cells, the sinuses are larger and more numerous than in the peripheral portions of the node.

The lymph vessels entering on the convex surface spread out in the cortex to form a rich plexus, the peripheral or cortical sinus. This continues in and around the follicles to the central portion, where it forms another plexus, the medullary sinus. The sinuses are broken up and penetrated by the reticular fibers, so that the entire mass of lymphoid tissue is interspersed by irregular, tortuous lymph spaces or sinuses, which, according to Maximow and Rössle and Yoshida, are lined, not by true endothelium, but by the flattened reticular cells. At the hilus, the lymph capillaries collect and pass out of the node as the efferent lymph vessels. The blood vessels, which enter and leave at the hilus, send branches into the follicles and medullary cords.

NORMAL PHYSIOLOGY OF THE LYMPH NODES

In all probability, the lymph nodes have many functions, only a few of which are known. Their rôle as hematopoietic organs is clear, and they are the means of formation of all types of lymphocytes. Other masses of lymphoid tissue which are found in the intestines, stomach, tonsils, pleura, liver and kidneys are not true nodes but also take part in this function.

The nodes are structures placed in the course of lymph vessels so that the lymph undergoes a filtration process as it percolates through the lymph sinuses. The phagocytic activity of the reticular cells in the sinuses points to this function. Particles of pigment, bacteria and tumor cells which in any way reach the lymphatic circulation are phagocytosed by the reticular cells.

As in other organs containing such histiocytes, the lymph nodes are believed by many to elaborate antibodies.

PATHOLOGY OF THE LYMPH NODES

The lymph nodes are most fully developed in young adult life and may undergo degeneration or involution in old age. As this paper is chiefly concerned with inflammatory reactions, other pathologic conditions, such as malformations, circulatory and metabolic disturbances and tumors, will not be considered. The works of Sternberg,[9] Aschoff,[10] Bell [11] and Zurhelle [12] have been freely consulted in this study.

9. Sternberg, C.: Die Lymphknoten, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 1, pt. 1, p. 256.

10. Aschoff, Ludwig: Lymphknoten pathologische Anatomie, ed. 7, Jena, Gustav Fischer, 1928, p. 126.

(Footnotes continued on next page)

Acute Nonspecific Inflammations.—The rôle of the nodes as filters brings about frequent inflammatory changes. Near the site of any acute inflammation in the body there appear pain and swelling of the regional nodes (acute lymphadenitis). The same condition can be caused, though less frequently, by hematogenous infection. The acutely inflamed nodes are enlarged in varying degree and appear bright red on the surface and on cut section. Although they are usually firm, they may become softened in inflammations of greater severity.

Histologically, it is noticed that the widening of the blood vessels often leads to hemorrhage within the node. The lymph sinuses are greatly dilated, and the reticular cells become swollen and may lie free in the sinuses, a condition which has been designated desquamative catarrh. Rössle and Yoshida noted stretching and tearing of the reticular fibers (*Gitterfasern*), which they believed caused softening of the node. In the early stages, the lymphoid elements may show only slight change, whereas later the germ centers enlarge and rapidly produce lymphocytes, causing a hyperplasia of the lymphoid tissue. Inflammatory changes may also be seen in the surrounding connective tissue and fat. This periadenitis is of varying degree, depending on the severity of the primary condition.

In acute inflammations, polymorphonuclear leukocytes are frequently seen in the lymph sinuses. In severe, purulent inflammations there may be a massive diapedesis of these cells from the vessels into the parenchyma of the node which result in purulent lymphadenitis. As a rule, this happens simultaneously in different parts of the structure, causing numerous small abscesses. This type of inflammation often leads to a suppurative periadenitis, which may penetrate to the outside, with the formation of a fistula. In phlegmons, decubital gangrene, gangrenous angina and any other foul, sanious inflammation, the entire node may be transformed into a putrid, greenish, necrotic mass in which many bacteria are found. Healing occurs with scarring, and calcification may occasionally take place.

Chronic Nonspecific Inflammation.—As a result of repeated acute inflammations or mild irritations, chronic lymphadenitis may develop. It is frequently observed in the tracheal and bronchial nodes as a result of inspired pigment granules. The signs of acute inflammation may have been present only to a slight degree and remained in the back-

11. Bell, E. T.: A Text Book of Pathology, Philadelphia, Lea & Febiger, 1930, p. 413.

12. Zurhelle, E.: Histopathologische Studien an syphilitischen Lymphdrüsen des primären und sekundären Stadiums, Dermat. Ztschr. **34**:1, 1921; Zur Histopathologie der rezent syphilitischen Lymphdrüsenerkrankung, Deutsche med. Wchnschr. **38**:1, 1921; Die Histopathologie der rezent syphilitischen Lymphdrüsenerkrankung, Arch. f. Dermat. u. Syph. **38**:366, 1922; footnote 8.

ground. The gradual outcome is an increase in the connective tissue components and a diminution of the cellular elements of the node, although in the early stages there is lymphoid hyperplasia. The capsule and trabeculae become wider owing to the formation of new connective tissue, the reticular fibers increase in number and thickness, and finally there is a diffuse sclerosis of the entire structure which converts it into a fibrous mass. While this is happening, the lymphoid tissue gradually becomes less and less, and then may disappear entirely. Hyalinization may be observed in fibrous nodes, a process in which, according to Rössle and Yoshida, the reticular cells play an active part. They stated that hyalin is a secretory product of these cells. Calcification is also occasionally noticed.

In nonspecific chronic lymphadenitis tuberculoid reactions have been reported. In lymphogranuloma inguinale, a disease of unknown etiology, Zakon,[13] Sulzberger and Wise[14] and Sternberg noted epithelioid and giant cells in the affected nodes. Necrosis may also occur in some cases, so that the resemblance to a gumma or to tuberculous lymphadenitis is striking.

Tuberculous Lymphadenitis.—Tuberculous infection of lymph nodes may take place through the lymphatics which drain a nearby diseased focus, or the bacilli may gain entrance through the blood stream and involve lymphoid structures which have no direct relationship to a tuberculous process.

In the case of a primary tuberculous complex, which occurs rarely in the skin and accessible mucosae, a regional adenopathy is invariably present. This type of infection, which affects young children almost exclusively, takes place only in those previously nontuberculous, and has been compared when it occurs on the skin to the syphilitic chancre with its local ulceration and satellite adenopathy. In the past ten years this phase of cutaneous tuberculosis has been discussed by Krantz,[15] Bruusgaard,[16] Rotnes,[17] Bezecny[18] and others. All authorities believe that by far the greater number of examples of the primary complex occur

13. Zakon, S. J.: Lymphogranulomatosis Inguinalis or Durand-Nicolas-Favre Disease: Review of Literature and Report of Three Cases, Arch. Dermat. & Syph. **26**:238 (Aug.) 1932.

14. Sulzberger, M. B., and Wise, Fred: Lymphopathia Venerea, J. A. M. A. **99**:1407 (Oct. 22) 1932.

15. Krantz, Walter: Der tuberkulöse Primärkomplex an der Haut, Zentralbl. f. Haut- u. Geschlechtskr. **39**:1, 1931.

16. Bruusgaard, E.: Klinische Beiträge zur Pathogenese der Hauttuberkulose, Arch. f. Dermat. u. Syph. **152**:465, 1926.

17. Rotnes, P. L.: Tuberkulöser Primärkomplex auf der Haut der Erwachsenen, Dermat. Wchnschr. **95**:1605, 1932.

18. Bezecny: Tuberkulöser Primärkomplex der Haut, Dermat. Wchnschr. **96**: 58, 1933.

in the inner organs (lungs and gastro-intestinal tract), and that here, too, regional adenitis is a constant accompaniment. The cases of primary complex of the skin in which the affected superficial lymph nodes have been examined microscopically are few, but in all instances the observations were those regarded as typical of tuberculosis.

Wolff [19] mentioned numerous sharply demarcated miliary tubercles containing large numbers of giant cells which Löwenstein observed microscopically in the inguinal nodes of a patient with so-called circumcision tuberculosis a variety of the primary complex.

In describing a case of primary tuberculous ulcer of the cheek, Escherich [20] noted histologic evidences of tuberculosis in the cervical nodes.

Levy [21] made a microscopic diagnosis of caseating tuberculosis of the inguinal nodes which became involved secondary to a primary complex located in the perineal region of a 6 month old child.

Involvement of the regional nodes in inoculation tuberculosis, however, is not limited to the primary complex. There have been occasional reports which described such involvement following inoculation tuberculosis of the skin in patients with a previous demonstrable tuberculous infection, usually in the lungs.

Krantz stated that the case which Jadassohn described in Mracek's "Handbuch der Hautkrankenheiten," that of a patient, aged 20, with a tuberculous lesion of the arm and enlarged axillary nodes, was in reality an example of secondary infection, as evidenced by the insignificance and delayed appearance of the adenopathy, which nevertheless was microscopically tuberculous. Krantz also believed that several of the cases which Stokes [22] reported in 1925, in which there was adenitis following a cutaneous tuberculous lesion, were tuberculous infections of a secondary type.

Rochat [23] reported the case of a girl, aged 21, in whom a tuberculous ulcer of the hymen developed following intercourse with a man who had genito-urinary tuberculosis. The histologic study of the inguinal nodes showed caseation and tuberculoid structure. This case was not regarded as an example of the primary complex because of the history

19. Wolff, Ernst: Ueber Zirkumzisionstuberkulose, Berl. klin. Wchnschr. **58**: 1531, 1921.

20. Escherich, Theodor: Die Infectionswege der Tuberkulose, insbesondere im Säuglingsalter, Wien. klin. Wchnschr. **22**:515, 1909.

21. Levy, Siegfried: Zur Kasuistik der primären Hauttuberkulose, Beitr. z. Klin. d. Tuberk. **70**:784, 1928.

22. Stokes, John H.: Primary Inoculation Tuberculosis of the Skin with Metastasis to the Regional Lymph Nodes, Am. J. M. Sc. **169**:722, 1925.

23. Rochat, Paul: Etude des superinfections tuberculeuses de la peau (pseudo-complexes primaires). A propos d'une inoculation tuberculeuse de la vulve par contact sexuel, Ann. de dermat. et syph. **10**:369, 1929.

of tuberculosis in the patient's family and the presence of signs of previous tuberculosis in the lungs elicited by means of roentgen examination.

Cases of tuberculous lymphadenitis which involve nodes not in the drainage areas of other tuberculous foci are well known. The cervical nodes in children are relatively frequently affected in this type.

Histologically, the typical structure of all tuberculosis of the lymph nodes is a miliary tubercle, which contains giant cells and groups of epithelioid cells which enlarge and coalesce with one another. This early stage is similar to the tuberculoid reaction in the nodes in early syphilis.

As the process advances, caseation occurs in the center of the nodule. There may be only one epithelioid tubercle in the entire node, or the whole structure may be involved, with a conglomeration of tubercles and widespread caseous degeneration. Single tubercles can often be seen at the periphery of these degenerated areas. Hyalinization is frequently observed.

Sternberg discussed a peculiar form of reaction known as Ziegler's large cell hyperplasia. Here there is replacement of the lymphoid tissue throughout almost the entire node by lobules of spindle-shaped epithelioid cells with cords of lymphocytes interposed and only occasional giant cells. Sternberg regarded this reaction as a nonspecific response of the lining of the sinuses to irritation and stated that the diagnosis of tuberculosis was possible only when typical tubercles were found. This type of reaction is identical with that observed by Michelson in the nodes in early syphilis.

In 1904 Bartel [24] concluded from an investigation of tuberculosis in cattle that nodes which could transmit the disease to laboratory animals might even be negative for tuberculosis microscopically.

On the other hand, Jonske,[25] in 1909, was unable to substantiate this view after careful study, and although he admitted that gross evidences of the disease might be lacking, any node which could be proved to be tuberculous by inoculation into animals could be shown to be typically affected histologically.

Aschoff, basing his opinions on his wide experience, stated the belief that definite, typical histologic evidences of tuberculosis were present in all of the nodes which harbored the bacilli.

The Superficial Lymph Nodes in Syphilis.—Early Syphilis: The nodes in early syphilis were carefully studied by almost all of the older

24. Bartel, J.: Die Infectionswege bei der Fütterungstuberkulose, Wien. klin. Wchnschr. **17**:414, 1904.

25. Jonske, W.: Untersuchungen zur Frage des Vorkommens latenter Tuberkelbazillen in den intermuskulären Lymphdrüsen generalisiert tuberkulöser Rinder, Virchows Arch. f. path. Anat. **198**:563, 1909.

syphilologists, and more recently Zurhelle made an extensive investigation of these structures and reported his observations in detail.

The usual reaction of the lymph nodes to infection in newly acquired syphilis is banal or nonspecific, and there is nothing distinctive of that disease. The process is a chronic productive inflammation with hyperplasia of the lymphoid substance such as might occur in chronic irritation due to other causes. Zurhelle noted in the early stages of the process an edematous, inflammatory swelling of the capsule and trabeculae, with infiltration of lymphocytes, lymphocytic plasma cells and fibroblasts. He differentiated between lymphocytic and lymphoblastic plasma cells. The former is the ordinary type described by Unna in 1907, characterized by an eccentric nucleus, the chromatin of which is clumped and often in cart-wheel arrangement. Although its origin has been debated, it is thought to arise from the lymphocyte, and almost nothing is known as to its function. The lymphoblastic plasma cell, which Schridde first observed in the germ centers of hypertrophic tonsils, is a large cell which is differentiated from the pale red lymphoblast by its strikingly dark staining with methyl green pyronine. It is larger than the lymphoblast, and its nucleus, though similar in features to that of the lymphoblast, lies eccentrically at one pole of the cell and has a bright halo on the side where the largest amount of protoplasm is located. Zurhelle maintained that these cells, which are thought to arise from lymphoblasts, correspond to the lymphocytic plasma cells which arise from lymphocytes. He never observed a lymphocyte plasma cell which originated from one of the lymphoblastic type.

Zurhelle also noted an early increase of the cells in the germ centers of the follicles with transformation of the lymphoblasts to lymphoblastic plasma cells. At the periphery of the follicles these cells were uncommonly seen, and the smaller lymphocytic plasma cells were more frequent. Zurhelle further observed inflammatory changes in the lymph sinuses with immigration of lymphocytes. There were an endophlebitis and periphlebitis in the capsule and surrounding tissue, which eventually led in some cases to closure of the lumens of the vessels.

Rössle and Yoshida noted definite growth and thickening of the lattice fibrils in syphilitic nodes, which they felt was the chief factor in causing their induration.

In contrast to the usual banal reaction in early syphilis, Michelson, as previously mentioned, found a tuberculoid structure in about 25 per cent of the cases which he studied. In some, the lymphoid tissue of the entire node was almost entirely replaced by closely packed epithelioid cells compressed into lobules, which were separated by thin strands of lymphocytes. This structure was likened to that seen in the lupoid of Boeck. A second type was observed in which there were small collections of epithelioid cells containing one or more giant cells. This type

of formation superficially resembled the lesions of miliary tuberculosis, except that no necrosis was noted in any of the sections. Further examination showed in some cases the tuberculous reaction in the trabeculae in which the connective tissue was almost completely replaced by epithelioid and giant cells. The epithelioid germ center, in which there were concentrically arranged epithelioid cells in the center of the follicles, was also described.

Other observers have also noted evidence of the tuberculoid reaction in the nodes in early syphilis. In studying the regional nodes in experimental syphilis in rabbits, Graetz and Delbanco [26] found that, as in man, the lymph passages were attacked early and that the regional nodes soon became enlarged. On cut section some nodes presented nodules which gave the impression of small gummas. Microscopically, the usual observation was a simple hyperplasia, but in 1 case giant cells were noted in one portion, whereas the other areas showed only nonspecific inflammation.

In describing the pathologic changes of the primary syphilitic bubo, Power and Murphy [27] stated that large round cells which may contain several nuclei are occasionally seen. Saleeby and Greenbaum [28] removed the inguinal nodes from 21 patients with untreated syphilis and found the tuberculoid reaction in 3 cases of secondary syphilis.

Stoeckenius [29] studied the lymph nodes in 4 cases of newly acquired syphilis which came to autopsy from other causes. In most sections he found the banal type of inflammation, but he also observed giant cells of the Langhans type. He did not, however, encounter caseation or collections of epithelioid cells.

Late Syphilis: True gumma of the lymph nodes is a rare manifestation of syphilis and is frequently diagnosed incorrectly. Zurhelle stated that Fournier found no cases of gummas of the lymph nodes in 3,249 patients with tertiary syphilis. The statistics of all observers are similar from the standpoint of rarity. Löwenbach,[30] Fasal,[31] Wile [32] and others

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26. Graetz, F., and Delbanco, E.: Weitere Beiträge zum Studium der Histopathologie der experimentellen Kaninchensyphilis, Dermat. Wchnschr. **58**:6, 1914.

27. Power, D'Arcy, and Murphy, J. K.: A System of Syphilis, New York, Oxford University Press, 1908, vol. 1, p. 157.

28. Saleeby, E., and Greenbaum, S.: Comparative Biologic and Histiologic Study of Lymph Glands from Syphilitic Patients, J. A. M. A. **96**:98 (Jan. 10) 1931.

29. Stoeckenius, W.: Beobachtungen an Todesfällen bei frischer Syphilis, Beitr. z. path. Anat. u. z. allg. Path. **68**:135, 1921.

30. Löwenbach, G.: Beitrag zur Histologie der gummösen Lymphome, Arch. f. Dermat. u. Syph. **48**:71, 1899.

31. Fasal, H.: Zur Kenntnis der gummösen Lymphome, Arch. f. Dermat. u. Syph. **103**:305, 1910.

32. Wile, U. J.: Gummata of the Superficial Lymph Nodes with Report of a Case, Arch. f. Dermat. u. Syph. **113**:1193, 1912.

have discussed the condition, and more recently Cummer [33] reviewed its clinical aspects from an analysis of 86 cases.

The condition occurs with equal frequency in both sexes and has an extremely variable symptomatology, characterized usually by indolent, enlarged nodes or groups of nodes, a positive Wassermann reaction, the occasional formation of sinuses and the presence of punched-out, serpiginous ulcers on the surface of the overlying skin. As a rule, surgical therapeutic measures result in delayed healing or lack of healing, but the process responds rapidly to antisyphilitic drugs.

The histopathologic changes of gummatous lymphadenitis are variable. In a case studied by Zurhelle there was only a nonspecific hyperplasia of the node such as is seen in secondary syphilis.

Löwenbach, on the other hand, observed an almost complete absence of normal lymphoid tissue, with replacement by a peculiar granulation tissue containing large numbers of pale, giant and endothelial-like cells, which called to mind sarcoma or endothelioma. Sternberg later expressed the opinion that this was perhaps a case of Hodgkin's disease in a syphilitic patient.

Fasal noted an infiltrate in the node which was composed of plasma and epithelioid cells, with an occasional giant cell. In the deeper portions of the node there was beginning necrosis. He believed that the tendency toward the formation of young connective tissue, which was less noticeable in tuberculous nodes, spoke for gumma, but he concluded that the histologic study was difficult and the results not always conclusive.

Michelson reported the histologic changes in 2 cases of gummatous lymphadenitis. In both there were areas of liquefaction necrosis in addition to plasma cells, polymorphonuclear leukocytes and a few epithelioid cells in the sections, though there was little similarity to the type of reaction which was observed in the cases of early syphilis.

Aschoff stated that the observation of endarteritis and endophlebitis obliterans in the tissues surrounding the involved nodes aided in the diagnosis.

From a consideration of the foregoing opinions, it may be seen that the histopathologic changes of gummatous lymph nodes are inconstant and inconclusive and therefore difficult to diagnose. The similarity of caseating tuberculosis, as in the cases described by Michelson, may be striking, and in most instances the microscopic examination merely serves as an additional aid in the formation of a diagnostic opinion.

RESULTS OF STUDIES OF THE TUBERCULOID REACTION

The material for this study was obtained from the Minneapolis General Hospital, the University of Minnesota Hospital, the St. Paul

33. Cummer, C. L.: The Lymphadenitis of Tertiary Syphilis with Survey of the Literature, Am. J. Syph. **12**:13, 1928.

City Hospital and the Glen Lake Sanatorium for tuberculosis. All of the nodes which were examined were fixed in 70 per cent alcohol or 10 per cent formaldehyde and stained with hematoxylin and eosin.

As a basis for comparison, nodes were obtained which had been removed in cervical and axillary dissections from 55 patients with carcinomas of the lower lip and breast who had neither clinical nor histologic evidences of metastasis. So far as could be determined, the nodes were normal, and in no case was an infectious process evident. Several nodes from each patient were examined.

The nodes which had been affected following one of the so-called nonspecific infections were then studied. This group of 16 cases included acute pustular dermatitis, infection of the upper respiratory tract, ecthyma vulgaris, acne conglobata and chronic dermatitis complicated by pyodermia. The specimens were obtained from the inguinal, axillary, epitrochlear or cervical regions, depending on the location of the primary condition.

TABLE 1.—*Summary of Histologic Study of Nodes*

	Total Number of Patients	Banal	Tuberculoid
Normal nodes	55	55	..
Nonspecific infections	16	16	..
Syphilis	70	59 (84.3%)	11 (15.7%)
Negative Wassermann reaction	8	8	..
Positive Wassermann reaction	62	51	11

The group from the tuberculous patients included 1 enlarged inguinal node from a case of primary tuberculous ulcer of the ankle (primary complex), as well as 49 nodes from 25 patients who had pulmonary, intestinal, renal or other forms of visceral tuberculosis and who had succumbed to the disease or its complications. The latter nodes were excised from the inguinal regions at autopsy and in most instances were removed bilaterally. All appeared normal on gross examination and on cut section, and none were in the drainage areas of an open or active tuberculous focus.

Finally, a palpable, enlarged node was excised under local anesthesia from each of 70 patients with undoubted syphilis during the active primary or secondary stages in which treatment was not being given. The great majority of the specimens were removed from the inguinal region, although in a few instances cervical, axillary or epitrochlear nodes were excised from patients presenting the generalized adenopathy of secondary syphilis.

A summary of the histologic study of these nodes to determine the presence of the tuberculoid reaction is given in table 1.

COMMENT

The kind of response of any tissue to infection may be broadly designated as banal or tuberculoid, and no single factor entirely governs its type. The invading organism is of prime importance, as shown by the fact that tuberculoid structure occurs only in a few inflammatory processes among which are tuberculosis, syphilis, leprosy and fungus infections, while in other infectious diseases, such as those caused by staphylococci and streptococci, nonspecific inflammatory changes are almost constant regardless of the chronicity of the process.

In spite of the type of invading organism, tissue susceptibility and capability of reaction are also of great importance, and these factors in turn are intimately associated with the immunologic reactions of the host. Thus the same agent may give rise to reactions which histologically vary from the most banal to those which are characteristically tuberculoid. The correlation of numerous observations regarding these facts formed the basis of the Lewandowsky [34] law which states that infectious diseases in general are characterized by a banal type of inflammation during which the organisms multiply in the body unhindered, whereas a tuberculoid structure may appear if the invaders are subjected to the action of the antibodies.

The origin of the various elements making up the tuberculoid structure, and especially that of the epithelioid cells, cannot be considered as definitely settled, even though there has been extensive investigation of the question, which has been well summarized by Maximow.[35]

The contention that epithelioid cells originated exclusively from blood leukocytes was supported by Cohnheim, R. Koch, Metchnikoff and Borrel, while Baumgarten, Orth and other German investigators traced them exclusively to the fixed, local elements of the tissue. Still others assigned their origin to blood lymphocytes, whereas Castren believed that in tuberculosis of human connective tissue the epithelioid cells originated chiefly, if not exclusively, from the fibroblasts. Foot thought that they were derivatives of endothelium. The last mentioned view cannot be denied if the term endothelium is used to include the cells which line the venous sinuses of the spleen and the lymph sinuses of the nodes and the Kupffer cells of the liver, which take an active part in the formation of the tubercle. This usage of the term endothelium, however, is misleading, as the aforementioned cells are entirely different in function from the true endothelial cells which line ordinary blood and lymph vessels.

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34. Lewandowsky, F.: Die Tuberkulose der Haut, Berlin, Julius Springer, 1916, p. 55.

35. Maximow, A. A.: Rôle of the Nongranular Blood Leukocytes in the Formation of the Tubercle, J. Infect. Dis. **37**:418 (Nov.) 1925; Tuberculosis of Mammalian Tissue in Vitro, ibid. **34**:549 (June) 1924.

As early as 1902, Maximow stated that epithelioid cells are polyblasts of a special type, which in turn are cells having definite phagocytic properties, present in all of the inflammatory processes and derived from lymphocytes and local tissue cells. Later, by means of careful studies of tissue cultures of lymphoid tissue, omentum and loose connective tissue of adult rabbits, he definitely traced the development of all of the components of tuberculoid structure. The tissues were first cultivated under normal conditions, and the following cell types were observed: fibroblasts, endothelial cells lining blood vessels, reticular cells and lymphocytes. The same tissues were later cultivated with tubercle bacilli, and the response of the various cells to the infection was observed. He found that the bacilli did not cause degeneration and death of the cells, as always happens in cultures which are contaminated with saprophytic organisms such as streptococci and staphylococci, but that the two elements, tubercle bacilli and cells, grew and proliferated together. A series of definite, specific, reactive changes ensued, which gave an exact duplication of the tuberculous process as it occurred in vivo.

In lymphoid tissue the reticular cells were most active, and their transition into active phagocytic epithelioid cells could be seen. The lymphocytes also underwent hypertrophy from typical small cells into large, ameboid, phagocytic elements or polyblasts, indistinguishable from the same type of cell originating from the reticular cells. These altered lymphocytes later became true epithelioid cells. No evidence could be found which indicated that either fibroblasts or true endothelial cells took any part in the formation of epithelioid or giant cells.

The origin of giant cells from epithelioid cells is generally conceded, and only the mode of formation is debatable. The most common opinion is that amitotic division of the nuclei in the hypertrophying cell body is responsible. Others feel that the process is one of mitotic division, while the possibility of the fusion of single epithelioid cells has been, in general, unpopular. In tissue cultures, Maximow observed epithelioid cells which assembled in clusters and in many cases fused together to form giant cells of the Langhans type, apparently as a result of decreased surface tension in the protoplasm. The increase in the nuclei was thought to be due partly to amitosis.

The minute observations of the transformation of these cells through all of the various stages seems to be extremely convincing evidence as to the origin of the components of tuberculoid structure.

Williams [36] recently called attention to the fact that allergy and immunity do not necessarily run parallel, even though they are closely

36. Williams, C. M.: Cutaneous Manifestations of Allergy, Arch. Dermat. & Syph. **29**:333 (March) 1934.

related. In syphilis, for example, the chancre is the response of normal susceptible tissue to the infection and almost never shows a tuberculoid structure. In the active secondary stage there is an eruption, not of multiple chancres, but of macules or papules, signifying an altered tissue reaction or allergy. Still the immunologic processes are unable to destroy the invaders, and the body teems with spirochetes, tuberculoid structure, with the exception of the miliary follicular syphilid, being almost lacking. Later in the disease, even though the tissues are hypersensitive to the organisms and react far out of proportion to the number of spirochetes which are present, the immunologic processes are active, and the organisms are few. In the late cases tuberculoid structure is the rule rather than the exception.

The same phenomena are noted to a less extent in tuberculosis of the skin. When there are only little resistance and a fatal outcome, as in acute hemorrhagic miliary tuberculosis, there are countless organisms in the lesions with only banal inflammatory changes histologically. On the other hand, in lupus vulgaris and other types of cutaneous tuberculosis, in which the immune processes are presumably active, bacilli in the lesions are scarce, but the response of the tissues in established cases is characteristically tuberculoid.

Jadassohn [37] found that when tubercle bacilli were inoculated into the skin of the rat, an animal relatively immune to tuberculous infection and having tuberculin-neutralizing antibodies in the blood, the bacilli were soon altered or became attenuated in virulence, and a tuberculoid structure rapidly resulted in the lesion produced. In spontaneous lupoids in man, tubercle bacilli are absent in most cases, and the reaction to tuberculin, even in high concentration, is, as a rule, negative; yet there is a typical tuberculoid structure. The well known case of lupoid of Boeck, which Kyrle [38] observed from the onset, was characterized in the early stages by banal inflammation and many tubercle bacilli, whereas later in the disease, as the immune processes became active, there were a transition to the tuberculoid reaction and simultaneous disappearance of the organisms.

Aside from diseases caused by living bacteria, the tuberculoid reaction is occasionally found at the sites of trichophytin, tuberculin, luetin and other allergen tests, hence Wise and Sulzberger [39] preferred to enlarge the Lewandowsky law to include all noxious agents, rather than only living bacteria.

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37. Jadassohn, W.: Die Inokulationstuberkulose der Rattenhaut (Ein Beitrag zur Frage der Hauttuberkulose mit positiver Anergie), Arch. f. Dermat. u. Syph. **167**:169, 1932.

38. Kyrle, Josef: Histobiologie der menschlichen Haut und ihrer Erkrankungen, ed. 2, Berlin, Julius Springer, 1927, p. 198.

39. Wise, F., and Sulzberger, M. B.: The 1933 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, 1934, p. 229.

The correlation of histologic with clinical observations leads one to believe that in the skin at least there is a more constant parallelism between the tuberculoid reaction and immunity than between allergy and immunity, even though the relationships are variable, and that this type of structure signifies the activity of the protective mechanisms of the body.

The studies which form the basis of this paper allowed certain conclusions to be drawn, after due consideration of the fact that deductions which are too widespread cannot be made on any small group of cases.

The first examinations were made on apparently normal superficial regional lymph nodes which had been removed from patients with carcinomas of the lower lip and breast. Those which showed evidences of metastasis were not included in this study. No specimen showed tuberculoid structure, which leads one to believe that in normal lymph nodes that type of histologic structure is not found.

None of the nodes which were removed from patients with nonspecific infections showed evidence of the tuberculoid reaction, which conforms with the observations of others that a specific structure is rarely provoked by infectious processes other than tuberculosis, syphilis, leprosy and certain fungus infections.

The tubercle bacillus is known to produce this type of tissue reaction more consistently than any other organism. Whereas in syphilis the type of histologic response to the spirochete depends more on the reactivity of the tissues than on the organism, the opposite holds true in tuberculosis, in which the tuberculoid structure almost invariably appears sooner or later. True, there are cases in which the response is banal, as has been previously mentioned, but the property of the tubercle bacillus to provoke a specialized tissue response seems to be the factor of greatest importance.

The results of the study of the nodes which were excised from tuberculous patients were not given in table 1, because with the exception of the node from the case of primary tuberculous ulcer of the ankle, they were not in the direct drainage areas of an infectious process. The node in question, however, showed several typical epithelioid cell tubercles containing occasional giant cells, and in one area there was beginning caseation. The type of structure in this specimen could not be definitely differentiated from that which was observed in the nodes in early syphilis. Although no far-reaching deductions may be made from a single case, it is believed that in view of the observations of the workers who have in the past examined histologically the involved regional nodes in cases of primary and secondary inoculation tuberculosis, such nodes invariably present characteristic tuberculoid structure.

The study of the inguinal nodes from patients with fatal visceral tuberculosis was interesting. It was reasonable to assume that any

histologic change which coincided with that regarded as characteristic of tuberculosis should be considered as such, even though the node in question appeared normal on gross examination. In this group of 25 cases, definite clusters of epithelioid cells containing from one to several giant cells were found in 3 instances, 2 of which in addition showed caseation. In all of the others only the banal type of reaction was observed, and in most instances fibrosis and atrophy were present. These observations substantiate the views which were advanced many years ago by Pizzini,[40] Beitzke,[41] Bartel,[24] Jonske [25] and others, that tuberculous lymphadenitis is not always manifest on gross examination. As Michelson has pointed out, the tuberculoid reactions occurring in the nodes in early syphilis and in tuberculous lymphadenitis may be indistinguishable, the only difference lying in the lack of tendency to caseation in the nodes in early syphilis.

As is shown in table 1, definite tuberculoid structure was observed in approximately 16 per cent of this group, a result which is slightly lower but not essentially different from that which Michelson obtained. Although the 8 patients in this series for whom the Wassermann test of the blood was negative showed no evidences of tuberculoid structure, Michelson previously found in his investigation that a positive Wassermann reaction was not a prerequisite for the development of this type of structure.

Believing that such a study would be of interest, he also performed the Mantoux test in 65 of his patients. In the entire group, the percentage of positive tests was no higher than the average in nonsyphilitic persons, and the tuberculoid reaction occurred even less frequently in those having positive Mantoux tests. Luotest [42] was also used in 26 instances according to the technic of Müller and Brandt of the State Serum Institute of Vienna. While the results were entirely negative, 9 of the group presented tuberculoid structure in the nodes. Michelson showed that the patients were apparently not in such a state of hypersensitivity that they would react positively to luotest, as frequently occurs in tertiary syphilis.

Both the Mantoux test and luotest were employed in 64 of the 70 syphilitic cases which I studied, and the results are given in table 2.

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40. Pizzini, D. L.: Tuberkelbazillen in den Lymphdrüsen Nichttuberkulöser, Ztschr. f. klin. Med. **21**:329, 1892.

41. Beitzke, H.: Untersuchungen über die Infectionswege der Tuberkulose, Virchows Arch. f. path. Anat. **210**:173, 1912.

42. Luotest is the proprietary name for a product that Müller and Brandt of the serotherapeutic institute of Vienna have prepared. This product is an extract from the organs of animals infected with syphilis. It has not been accepted by the Council on Pharmacy and Chemistry of the American Medical Association (Michelson [2]).

There was no demonstrable relationship between the tuberculoid reaction in the nodes and either of the two tests. In this group the percentage of positive Mantoux tests is about average and does not appear to be affected by the type of histologic reaction in the nodes.

After a consideration of the general significance of the tuberculoid reaction, it is felt that in the lymph nodes in early syphilis it represents a proliferative response, chiefly of the reticulo-endothelial elements against the spirochete, and that it is probably closely related to the immunologic processes. To determine whether or not the tuberculoid reaction which occurs in the lymph nodes early in the course of a syphilitic infection is a manifestation of immunity so increased that the patient is more capable of withstanding the disease would require many years of observation of untreated patients who were known by histologic examination to have either a banal or a tuberculoid structure early in

TABLE 2.—*Results with Luotest and the Mantoux Test* *

			Banal	Tuberculoid
Syphilis (64 cases)	Mantoux test.....	Positive	14	1
		Negative	42	7
	Luotest.....	Positive	0	0
		Negative	56	8

* In the Mantoux tests, 0.1 cc. of a 1:1,000 dilution of old tuberculin was injected intradermally. A definite area of redness and induration at the site of injection in twenty-four hours was considered a positive result.

the disease. This is of course impossible. It was noted that in the group studied patients who showed the banal reaction responded as well to antisyphilitic therapy as did those in whom tuberculoid structure was found. This is probably of little significance in the analysis of the tuberculoid reaction, for the drugs used in the treatment of syphilis are so effective that the natural processes are not required to exert a primary influence.

SUMMARY AND CONCLUSIONS

This study of the superficial lymph nodes was made in order to determine, if possible, the significance of the tuberculoid reaction which occurs in the nodes of patients with newly acquired syphilis. To gain a better understanding of lymph nodes, their anatomy, physiology and pathologic changes in nonspecific infections, tuberculosis and syphilis were briefly reviewed.

Apparently normal, superficial nodes which were excised from 55 patients with carcinomas of the lower lip and breast were studied microscopically and compared with regional nodes which were removed from 16 patients with nonspecific infections and from 70 patients with early untreated syphilis. One inguinal node from a patient with a primary

tuberculous ulcer of the ankle and 49 nodes from 25 patients with fatal cases of visceral tuberculosis were also examined.

From an appraisal of the reports of other investigators and a survey of the results of this study, the following conclusions may be drawn:

Epithelioid cells in lymph nodes, according to the studies of Maximow on tissue culture, most likely originate from both reticular cells and lymphocytes. Giant cells, in turn, develop from epithelioid cells by fusion and amitotic division.

The tuberculoid reaction does not occur in normal nodes. In the group studied no section showed evidences of this type of structure.

The tuberculoid reaction in the lymph nodes in the group of so-called nonspecific infections is rare. In this series such histologic structure was not observed in nodes which were removed from patients with acute pustular dermatitis, furunculosis, pyodermia and similar conditions.

It is the opinion of competent observers that in all cases in which tubercle bacilli are present in the lymph nodes, specific tuberculoid structure appears, even though gross evidences of disease may be lacking. The latter fact was illustrated by the observation of microscopic tuberculous lymphadenitis in 3 of 25 patients in this study, who showed no gross manifestations of tuberculosis of the inguinal nodes. One inguinal node from a patient with a primary tuberculous ulcer of the ankle presented definite tuberculoid structure.

The lymphadenitis in early syphilis presents definite tuberculoid structure in approximately from 15 to 25 per cent of the cases, which may in some instances show all of the features which qualify a diagnosis of tuberculosis. In the group of 70 patients whom I studied, 15.7 per cent were found to have tuberculoid structure in the nodes. No parallelism between the tuberculoid reaction and the results with luotest or the Mantoux test could be shown.

Although this reaction is thought to be closely related to the immune processes of the body, its exact significance cannot be proved, owing to the long course of syphilis and the placing of all of the patients on an equal basis by chemotherapy. The clinical course of the disease indicates that the tuberculoid reaction is not a manifestation of precocious tertiarism or malignant syphilis.

There is not enough evidence to warrant a direct comparison of the reactivity of lymphoid tissue with that of the skin. If this could be done, however, the tuberculoid reaction might be considered an index to a higher degree of immunity than was possessed by patients who presented only banal inflammatory changes in the nodes.

In conclusion, from my studies of the tuberculoid reaction in lymph nodes, I believe that the reaction may be looked on only as a particular response against an invader, and that it does not possess the immunologic significance that it has when present in the skin.

EPIDERMOLYSIS BULLOSA ACQUISITA

SUCCESSFUL TREATMENT WITH IRON CACODYLATE, A BLOOD COAGULANT, CALCIUM (WITH PHOSPHORUS) AND ROENTGEN RAYS

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The following case is reported in the hope that the therapy found effective in it, at any rate temporarily, may be tried by others not only in the acquired but also in the hereditary type of epidermolysis bullosa.

REPORT OF A CASE

T. F. C., a white man, aged 58, a stationary engine fireman, was referred to me with a chronic, distressing and apparently baffling condition of the hands. It had been diagnosed as ringworm and treated for a year by six different members of a governmental medical corps; as eczema and treated for a dozen years or more by six or seven general practitioners; as old-fashioned eczema and treated at a dispensary, and as dermatitis venenata and treated by a dermatologist. The patient had received only slight transient relief.

Inquiry elicited the following: The family history was unimportant. During his boyhood the patient had measles and chickenpox; at 19, mumps, with severe orchitis; at 28, gonorrhea, with uneventful recovery, and several years before consulting me, hemorrhoids and an anal fistula, both relieved by operation. The skin was normal until the thirty-eighth year, when vesicular and exfoliating lesions, following slight accidental trauma, began to appear on the dorsa of the hands and the fingers and on the thenar eminences. The rest of the palms, the volar surfaces of the fingers and the mucosa were unaffected. The skin over the ankles was said to have been involved years before, but at the time of my examination it bore only superficial scars. For fifteen years, the lesions disappeared spontaneously with the approach of summer, but during the five years preceding my examination they had been constant.

Questioning and observation established the fact that if the skin of the hands was accidentally or purposely struck, rubbed or otherwise traumatized with a blunt instrument there occurred, in the following phenomenal sequence: (*a*) redness, (*b*) burning, (*c*) itching, (*d*) vesiculation—blisters exuding a viscid orange-colored fluid when broken—(*e*) exfoliation and (*f*) ulceration, the last two attended by smarting. Four or five hours elapsed between trauma and vesiculation. After healing, slightly rough, faintly pigmented superficial scars remained.

The urine was essentially normal. The Wassermann and the Kahn reactions of the blood gave negative results. The blood picture was: hemoglobin, 82 per cent (Dare); red cells, 4,100,000; white cells, 7,800; polymorphonuclears, 76 per cent; lymphocytes, large and small, 23 per cent; mononuclears, 1 per cent. The phytopharmacologic test, twice performed through the courtesy of Dr. Pels,[1] gave

1. Pels, I. R., and Macht, D. I.: Phytopharmacologic Examination of the Blood in Pemphigus and in Some Other Diseases of the Skin, Arch. Dermat. & Syph. **19**:640 (April) 1929; Phytopharmacology of Pemphigus and Other Dermatoses: Additional Studies, ibid. **23**:601 (April) 1931; Phytopharmacologic Test in Dermatology: Further Studies and Some Critical Estimations, ibid. **29**:206 (Feb.) 1934.

a toxic reading of 50 per cent on both occasions. There was an interdigital dermatitis of the feet, and scrapings on direct examination showed plentiful hyphae. Examination of scrapings from the hands gave negative results. The results of the trichophytin test (0.1 cc. of a 1 : 10 dilution) were positive.

Considering the history, the laboratory findings and the fact that the lesions on the hands bore little resemblance to "mycids" or to the lesions of any of the other dermatoses that had been identified with the case, the diagnosis of ringworm (of the feet) and of epidermolysis bullosa acquisita (of the hands) was made.

As it was considered possible that the patient's allergic state (positive trichophytin test) might be a factor in the production of the painfully annoying condition of the hands, desensitizing intradermal injections of trichophytin (1 : 50) were begun, but were abandoned with the seventh treatment (1 : 30) because it was believed that they were aggravating the lesions of epidermolysis.

Ten days before, with the thought that, as my case of epidermolysis bullosa acquisita had given approximately the same phytopharmacologic reading as pemphigus, the two diseases may be etiologically related, and knowing that Davis [2] and others had achieved a notable degree of success in pemphigus with iron cacodylate, sodium arsenate and a blood-coagulating preparation, I resolved to try that therapy, despite the gloomy prognostications as to epidermolysis bullosa in every textbook and article in which I had sought encouragement. Accordingly, intravenous injections of iron cacodylate and hypodermic injections of a blood-coagulating preparation were begun. Of the former, the dosage ranged from the initial dose of 0.03 Gm. to the maximum of 0.13 Gm., at from one to three day intervals. The dose of the blood coagulant was 1.5 cc. throughout. To this therapy, in view of the serous exudative process in epidermolysis bullosa, I added calcium (with phosphorus) by mouth, using an organic calcium-phosphorus concentrate. Local treatment at first included protective, soothing, antipruritic and supposedly epithelizing agents, but was soon restricted to a simple keratoplastic ointment. It is believed that some of the applications, though mild, were responsible for exacerbations of the eruption and for delaying the ideal result finally obtained.

In the sixth week of therapy (the third week of treatment with iron cacodylate, the blood-coagulating preparation and calcium), although considerable improvement was evident in both hands, it was decided to add roentgen rays to the therapy for one hand, leaving the other hand unirradiated as a control. A qarter unit dose of unfiltered roentgen rays was given to the right hand only. The iron cacodylate and the blood-coagulating preparation were then given every other day. Several days after the increase in dosage, both hands showed more improvement than they had shown at any time during the previous six weeks. This fact was gratefully noted by the patient, who for the first time in many months was able to sleep without disturbance from burning and itching. Ten days after the increase in dosage and after only two quarter unit doses of roentgen rays, the right hand showed only two lesions, the size of split peas, and healing, and was free from subjective symptoms. Twenty days after the increase of iron cacodylate and the blood-coagulating preparation and after only three quarter-unit treatments with roentgen rays were given, the right hand was objectively and subjectively normal. When the larger dosage of iron cacodylate and the blood-coagulating preparation had been given for five weeks, the left hand,

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2. Davis, R. H.: Treatment for Pemphigus, Arch. Dermat. & Syph. **3**:451 (March) 1929.

which had markedly improved without roentgen treatment, still occasionally showed a few lesions and gave some trouble from smarting. It was given a quarter unit dose of unfiltered roentgen rays. Nine days later, or a little more than six weeks after the increase in dosage of iron cacodylate and the blood-coagulating preparation, and after only two quarter unit doses of roentgen rays, the left hand was objectively and subjectively normal.

The iron cacodylate was continued, in decreased dosage, at intervals of four days for another month, when the patient was discharged with both hands normal for the first time in five and one-half years, with 10 pounds (4.5 Kg.) of additional weight and with more gratitude than I had ever before witnessed in a patient.

SUMMARY

The successful treatment of epidermolysis bullosa acquisita of twenty years' duration with iron cacodylate, a blood-coagulating preparation, calcium (with phosphorus) and roentgen rays is reported.

COMMENT

1. As dermatologic literature has little to offer in the way of treatment for the disease mentioned, and as the therapy tried by me is evidently effective, at least temporarily, I believe that it is worthy of further trial.

2. The desirability of increasing the iron cacodylate to the maximum as soon as tolerance becomes apparent is suggested.

3. Local treatment should be restricted to protective and keratoplastic agents and a minimum of roentgen radiation.

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DANLOS SYNDROME ASSOCIATED WITH CONGENITAL LIPOMATOSIS

NORMAN TOBIAS, M.D.
ST. LOUIS

Margarot [1] defined the Danlos syndrome as a tetrad of symptoms consisting of: (1) hyperelasticity of the skin; (2) hyperlaxity of the joints; (3) fragility of the skin, involving especially the exposed surfaces and prominences, and (4) pseudotumors following trauma. While isolated cases exhibiting one or more of the characteristics have been described, the complete syndrome rarely occurs. No cases have been reported in the American literature. The incomplete cases consisting of cutis laxa or hyperflexibility of the joints alone may be classified as formes frustes.

REPORT OF A CASE

History.—M. G., a white girl, aged 9, was admitted to the pediatric division of St. Mary's Hospital for a tonsillectomy. She weighed 45½ pounds (20.6 Kg.), and the pulse rate and temperature were normal.

Birth was normal. She began to talk at 1½ years and walked at 2. Dentition appeared at 7 years. The child's intelligence was normal. She had varicella at the age of 5 and a fractured right thoracic rib at 7. The mother stated that up to the age of 2 the patient had "spells" of cyanosis which appeared and disappeared spontaneously. The extremities were chiefly involved at that time. It was also noticed that the child's skin was extremely fragile and that the slightest injury caused it to split, leaving disfiguring scars. At this time the mother while bathing the girl discovered "knots" in the deep subcutaneous tissue over the calves, arms and buttocks.

No hereditary history of the condition could be discovered. The parents, a brother and two sisters, were normal in every respect.

Physical Examination.—The child was a brunette with a slight frame and small features. The hair was dark brown, straight and normal in distribution and amount, but silky to the touch. The nails were normal except for longitudinal striations. The teeth were regular, dentition was normal, and there were no defects.

The skin had a peculiar velvety texture. It glided easily over the underlying structures. The bony prominences were readily felt because of a decrease in subcutaneous fat. A few dilated capillaries were present on the cheeks. Over the anterior portion of the chest and trunk small venules were visible.

Numerous scars were present resulting from slight injuries. At no time had bullae followed trauma, but a "splitting of the skin" occurred followed by

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From the Department of Dermatology and Syphilology, St. Louis University.

1. Margarot, J.; Deveze, P., and Coll de Carrera: Hyperlaxité cutanée et articulaire (syndrome de Danlos) existant chez trois membres d'une même famille, Bull Soc. franç. de dermat. et syph. **40**:277 (Feb.) 1933.

Fig. 1.—Cutis laxa. The retracted skin falls into place when released. Notice the scars on the forehead.

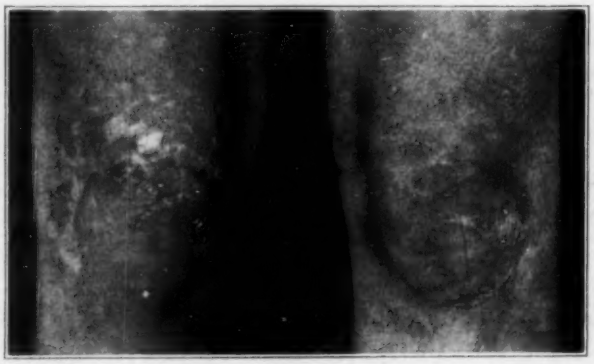

Fig. 2.—Characteristic scars on the knees following slight trauma.

"bruises." On the forehead were several longitudinal, irregular, cream-colored scars. Over the prominences of the elbow joints and knees were numerous soft, depressed, violaceous, atrophic scars resembling waffle markings. The skin over the tibias and ankles was also covered with depressed cicatrices of a pinkish hue.

The joints of the thumbs, fingers and wrists could easily be hyperextended. The index finger could be hyperextended to touch the dorsal surface of the hand. Direct traction on the metacarpophalangeal joints stretched the capsule and permitted an extension of 3 cm. The hyperlaxity was most marked in the joints of the thumbs.

Hard, smooth, shotlike, subcutaneous tumors could be felt anteriorly over the fibulas and posteriorly on the arms, forearms, buttocks and calves. They were not attached to the skin and were fully movable in the subcutaneous tissues.

Fig. 3.—Laxness of the joints with hyperextension of the fingers.

The hyperelasticity of the skin, which was general and bilateral, was more marked in the skin of the cheeks, thighs and legs when stretched. The comparative tabulation shows the difference in elasticity between the skin of the patient and that of a normal child.

	Patient, Cm.	Normal Control, Cm.
Cheek	2.5	1.7
Chin	1.5	1.2
Arm	3.0	1.6
Forearm	4.2	1.5
Thigh	4.6	1.5
Leg	4.6	1.0
Neck	2.5	1.5

Course.—The case was under observation for two years. No new lipomas developed. On a diet high in fat the patient gained about 4 pounds (1.8 Kg.).

On Nov. 10, 1933, she bruised her right elbow in a fall, and two days later a light blue oval tumor, 1 by 1½ inches (2.5 by 3.8 cm.), resembling a hematoma, developed on the tip of the right elbow. It was the size of a large walnut, not

tender and fairly soft. This was the first time that I had observed one of the pseudotumors first described by Danlos. A tight dressing applied over the lesion was followed in two weeks by complete absorption. The lipomas did not increase in number and appeared to be smaller.

Laboratory Examination.—A throat culture was negative, and the reactions to the Schick and tuberculin tests were negative. The blood count showed: red blood cells, 3,000,000; white blood cells, 7,900, and hemoglobin content, 58 per cent (Dare). The differential count showed: stab cells, 4 per cent; segmented forms, 43 per cent; lymphocytes, 50 per cent; monocytes, 1 per cent; eosinophils, 1 per cent; basophils, 1 per cent, and reticulocytes, 0.4 per cent. The color index was 1. The fragility test showed initial hemolysis in 0.42 and complete in 0.34 per cent of sodium chloride. The blood platelet count was 220,000. Blood chemistry showed: serum calcium, 6.4 mg. per hundred cubic centimeters; phosphates, 4.2 mg.; creatine, 1.2 mg.; creatinine, 9.6 mg.; nonprotein nitrogen, 36 mg., and sugar, 100 mg.

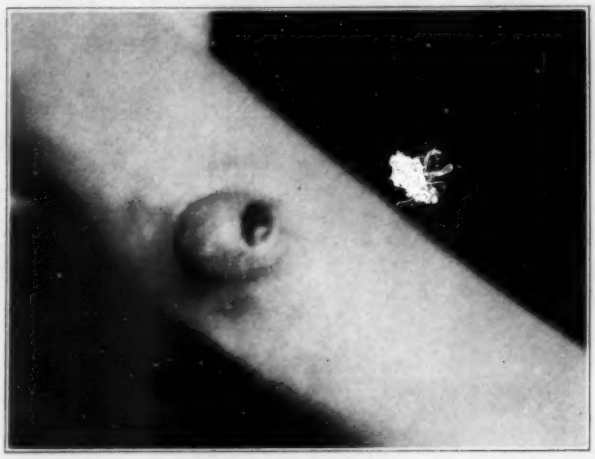

Fig. 4.—Pseudotumor on the posterior surface of the right elbow. There is a small area of superficial ulceration on the surface of the lesion.

The icterus index was 6. The van den Bergh test (both direct and indirect) gave negative results. The Wassermann and Kahn reactions of the blood were negative. The basal metabolic rate was plus 15, and the blood pressure was 114 systolic and 68 diastolic. The urine was normal. A roentgenogram of the long bones failed to show any evidence of pathologic changes or abnormality, and there were no unusual calcareous deposits. Roentgenograms of the skull and chest revealed no abnormalities.

Biopsy Examination (Dr. Collier).—Sections were embedded in paraffin, and three groups of stains were used: hematoxylin and eosin, Verhoeff's stain for elastic tissue and van Gieson's stain for collagen fibers.

Skin: Sections demonstrated a skin of unusual thinness with a stratum corneum having an average thickness of 4 cells and an underlying corium about half the normal thickness. There was no appreciable abnormality of the epithelial cells. The corium contained three or four times the normal number of elastic fibers. These fibers seemed to be more delicate and more branching than those usually

found in normal skin and the collagen fibers appeared more compact but less dense. In place of the loosely woven but thick bundles of collagen fibers there was fine meshed, well separated, fibrillar structure. The fibrils seemed to maintain their identity rather than to form bundles, which usually showed a tendency toward hyalinization. The elastic fibers mixed diffusely with the collagen fibrils.

There was a superabundance of sweat glands coiled in masses two or three times the size usually found. There was no cellular reaction about any of the integumental structures. The vessels appeared to have unusually large lumens and thin, almost insufficient-looking walls.

Lipomas: Sections of fatty material showed well defined fibrous capsules about each round or oval fat lobule. The capsules contained mostly collagen fibers, but

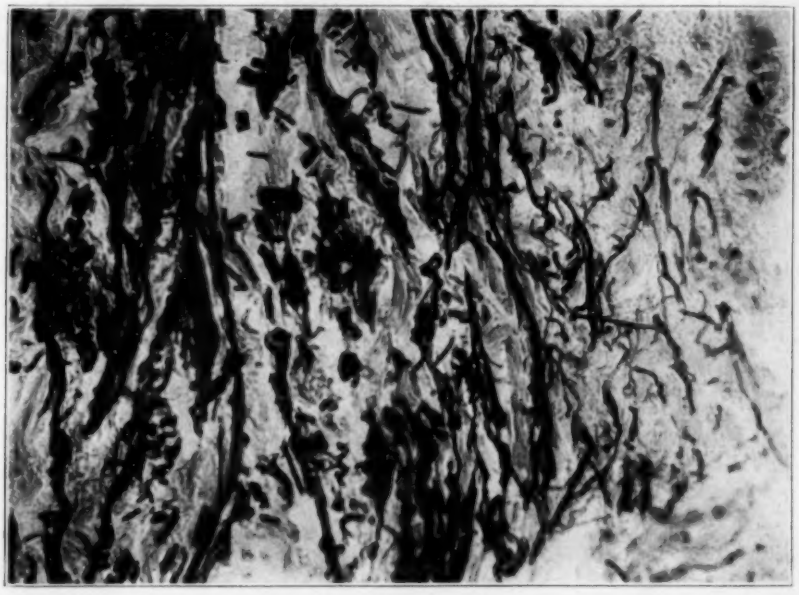

Fig. 5.—Hypertrophy of the elastic tissue fibers in the lower corium. There is some fibrillation and fragmentation.

also a few scattered elastic fibers. The fat cells within the lobules were normal for the most part, although some were filled with a material looking more mucoid than like true fat. There was no wandering cell reaction. The vessels appeared to be more abundant than one would expect in the interstitial capsules of the lobules.

REVIEW OF THE LITERATURE

The Danlos syndrome was first described by Hallopeau and de Lépinay [2] in 1906, although they did not recognize the true significance of the tumors and erroneously named them juvenile pseudo-

2. Hallopeau and de Lépinay, M.: Sur un cas de xanthome tubéreux et de tumeurs juveniles offrant les caractères du xanthome diabetique, Bull. Soc. franç. de dermat. et syph. **17**:283, 1906.

diabetic xanthoma. Two years later Danlos [3] saw the same patient, and from his study of the case arrived at a totally different conclusion. The icterus present, he believed, had no connection with the "xanthoma" lesions, and the scars over the prominences were not due to resorption of the "xanthomatous" tumors but were the result of trauma followed by suppuration, leaving a temporary yellowish tint to the scars which later assumed a violaceous hue. He also contended that the lesions were not caused by a pancreatic disturbance, and focused attention on the hyperelasticity of the skin which Hallopeau and de Lépinay had minimized in their study of the case. The "xanthoma" lesions decreased in size with rest and compression, an important point in his argument. Pautrier [4] performed biopsies on the tumors and found no xanthomatous cells, but only loose cellular tissue and dilated blood vessels, the pathologic process resulting from trauma with an abundant circumscribed outpouring of blood, the formation of a pocket and the infiltration of blood into the distended skin.

Schulmann and Lévy-Coblentz,[5] in 1932, reported a case presenting the syndrome in a girl 25 years old, with generalized cutis laxa, articular laxity, especially of the metacarpophalangeal joints, and violaceous flabby, soft, raisin-like tumors on the elbows and fingers. They felt justified in attaching the name of Danlos to the syndrome which he was the first in France to describe and identify. Recently Navarro Martin and Aguilera Maruri [6] reported an incomplete case in a man, aged 38, the interesting feature of which was the presence of hard, fibrous nodules in the region of the atrophic scars on the arms and elbows. The articular laxity was missing. Gilbert's [7] case in a man, aged 22, revealed formes frustes in other members of the family. The father and a sister of the patient presented only laxity of the joints, while two other sisters had acrocyanosis, a symptom which often occurs

3. Danlos, M.: Un cas de cutis laxa avec tumeurs par contusion chronique des coudes et des genoux (xanthome juvénile pseudo-diabetique de Hallopeau et de Lépinay), Bull. Soc. franç. de dermat. et syph. **19**:70 (Feb.) 1908.

4. Pautrier, M.: Note histologique sur un cas de cutis elastica avec pseudo-tumeurs aux genoux et aux coudes, Bull. Soc. franç. de dermat. et syph. **19**:72 (Feb.) 1908.

5. Schulmann, E., and Lévy-Coblentz, G.: Hyperélasticité cutanée (cutis laxa) et laxité articulaire avec fragilité anormale de la peau et tumeurs molluscoïdes post-traumatique (syndrome de Danlos), Bull. Soc. franç. de dermat. et syph. **39**: 1252 (July) 1932.

6. Navarro Martin, A., and Aguilera Maruri, C.: Un caso de cutis laxa y lesiones atróphicas de tipo eritromiélico, Actas dermo-sif. **25**:126, 1932.

7. Gilbert, A.; Villaret, M., and Bosviel, G.: Sur un cas d'hyperélasticité congénitale des ligaments articulaires et de la peau, Bull. et mém. Soc. méd. d. hôp. de Paris **49**:303, 1925.

in cutis laxa. Burrows,[8] in 1932, reported a case in a girl, aged 14, which cannot be classed under the Danlos syndrome because of the absence of tumors, although bullous lesions followed trauma. Acrocyanosis was present. The hereditary nature of the condition was shown in the father and sister, both of whom had laxity of the joints of the thumbs. Margarot would probably classify these cases as formes frustes. Cockayne [9] also described a case belonging to this group. His patient was a girl, 14 years old, who had cutis laxa and superficial bruises after trauma. There was also laxity of the joints. Mitral stenosis was present, but there was no history of acrocyanosis. Schubert's [10] case, in a man of 20, should be classified as belonging to the Danlos syndrome, although the author suggested the possibility of myotonia congenita as the diagnosis.

CLINICAL DESCRIPTION

The various components of the Danlos syndrome require discussion and description, as there is some variability in their appearance.

Cutis Laxa ("Gummi Haut," "India Rubber Skin").—This congenital condiiton which usually makes its appearance in the first decade of life consists of hyperelasticity of the skin with spontaneous retractability which is complete. This differs from the incomplete retractability, often unilateral, occurring in Recklinghausen's disease as dermatolysis. Clinically the skin appears smooth and velvety and feels soft. It is easily picked up in folds like accordion plaits. There is usually an associated hypervulnerability, with a tendency to the formation of hematoma, bruises, nodular swellings, bullous formation, splitting of the skin or ulceration followed by irregular atrophic scars. The cicatrices which follow splitting are usually linear, while those following bruises are characteristically waffle-like, similar to wrinkled silk, or striated. Hypotonia of the striated muscles and hyperflexibility of the joints, especially of the metacarpophalangeal joint, are often associated. Various endocrine and nerve anomalies may coexist.

Congenital defects often being multiple, the following associated lesions have been described in cases of cutis laxa: lymphangiectatic tumors (Cohn [11]), syringomyelia (Joederns [12]), Recklinghausen's disease

8. Burrows, A.: Epidermolysis Bullosa with Cutis Hyperelastica, Proc. Roy. Soc. Med. **25**:1319, 1932.

9. Cockayne, E. A.: Inherited Abnormalities of the Skin and Its Appendages, New York, Oxford University Press, 1933, p. 117.

10. Schubert, P.: Cutis laxa, Deutsche dermat Gesellsch. d. tschechoslav. Republ. **25**:634 (Dec. 7) 1924.

11. Cohn, P.: Demonstration eines Patienten mit Gummihaut, Verhandl. d. deutsch. dermat. Gesellsch. **9**:334, 1907.

12. Quoted by Bielschowsky.[16]

(Kozevnikow [12]), supernumerary teeth (Gilbert [7]), fibromas (Navarro Martin [6]), fibrous tumors and nevi (Margarot,[1] Siemens [12]), acrocyanosis (Burrows,[8] Joerdens,[12] Gilbert,[7] including three sisters of Gilbert's patient) and clubfoot (Hallopeau [2]). In Margarot's [1] cases the patients were below par in mental development.

The hereditary nature of the condition is not always apparent, although according to Kopp [13] it is an incomplete dominant characteristic. Hyperlaxity of the joints and acrocyanosis may appear in other members of the family as formes frustes. In Kopp's case the disease appeared in a man and his son, and in Margarot's cases in a man and his two sons.

The etiology of the condition is well summarized by the term, "constitutional mesenchymatosis" of congenital origin as used by Hirszfeldowa.[14] Burrows suggested that the endocrine glands controlling the development of connective tissue are at fault; Schubert suspected a relation to myotonia congenita, while Kopp pointed to atavism as a possible factor. Regarding the Danlos syndrome in its entirety, most authors agree that it is a form of Recklinghausen's disease involving the elastic tissues instead of the fibrous tissues. Grön's [15] formes frustes of neurofibromatosis have no connection, of course, with cutis laxa. Bielschowsky's [16] studies of sections showed neuromas of the cutaneous nerve endings. Clinically, the hereditary nature, the presence of fibromas and other nevic conditions strongly suggest this conclusion as brought to the attention by Margarot's and Navarro Martin's cases.

In my case there was associated lipomatosis, which belongs to the broad group of nevi, as shown by Gougerout and Salles.[17] When extensive, the nevi fit in with the clinical conception of Recklinghausen's disease. Furthermore, Adair [18] showed that these tumors are histogenetically related to the nervous system. It is therefore evident that lipomatosis may exist in the Danlos syndrome as part of the variable picture of mesenchymatosis.

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13. Kopp: Demonstration zweier Fälle von "Cutis Laxa," München. med. Wchnschr. **35**:259, 1888.

14. Hirszfeldowa, quoted by Steiner, K., in Jadassohn: Handbuch der Haut- und Geschlechtskrankeiten, Berlin, Julius Springer, 1932, vol. 4, p. 78.

15. Grön, K.: "Forme Fruste" of v. Recklinghausen's disease, Brit. J. Dermat. **35**:364, 1923.

16. Bielschowsky, F.: Beitrag zur Klinik und Pathologie der Lipatrophia circumscriptum (Cutis laxa), Deutsches Arch. f. klin. Med. **166**:96, 1930.

17. Gougerout, H., and Salles, P.: Théorie naevique des lipomatoses, Bull. Soc. franç. de dermat. et syph. **24**:363 (June) 1930.

18. Adair, F. E.; Pack, G. T., and Farrior, J. H.: Lipomas, Am. J. Cancer **16**:1104 (Sept.) 1932.

Hyperlaxity of the Joints.—The association of cutis laxa and articular laxity was first noted by Riehl in Riecke's textbook.[19] There are no reports available concerning the tissue changes in the joints, but it can be presumed that there is hyperplasia or hypertrophy of the elastic tissue fibers in the capsule or ligaments or both. The anomaly may be generalized or localized; the joints of the fingers and thumb are the usual sites. Luxations sometimes occur which are permanent. In one of Margarot's cases the clavicles were mobile because of the loose sternoclavicular articulations. There was an anterior luxation of the head of the radius. This was also present in the radiocubital joint. The hyperlaxity was most marked in the fingers, so that dorsal flexion was as great as palmar flexion. The knees showed a slight tendency toward laxity. In Schulmann's case the metacarpophalangeal and metatarsophalangeal joints could be easily disarticulated by a pulling traction, on release of which the joints would fall back into place.

Articular laxity has been present in all the cases showing the Danlos syndrome except in Navarro Martin's. It may exist as a dominant characteristic in the familial type and may not be associated with cutis laxa. The condition is never painful.

Epidermolysis.—The thinning of the entire epidermis and the almost total absence of subcutaneous tissue over bony prominences especially makes the skin liable to slight traumatic insult. Pinching the skin may result in an ecchymotic spot in a few hours. A blow which would not affect normal skin splits the skin and may result in a linear scar, an irregular ulceration or a pseudotumor composed of blood elements. Cicatrices are prone to occur over the bony prominences, especially the forehead, wrists, elbows, knees, anterior tibial surfaces and malleoli.

In some cases in which trauma does not produce hemorrhagic lesions, epidermolysis bullosa may occur. This condition was present in one of Gilbert's cases. Burrows reported a case in which bruises or blister-like lesions occurred after the slightest trauma. Acrocyanosis, cutis laxa and laxity of the joints were also present. In true cases of epidermolysis bullosa, cutis laxa is rare, although the opposite relation is not uncommon. This is difficult to explain, since the former condition is often associated with a lack of elastic tissue.

The scars are usually depressed and atrophic, but may be hypertrophic. The color varies from a pearly white to a violaceous hue. The latter predominates if acrocyanosis is present. Brownish pigmentation is not uncommon. The cicatrices on the elbows and other prominences often are irregular and have "waffle-like" or worm-eaten patterns. They are always soft and elastic and may contain telangiectasia.

19. Riecke, E.: Lehrbuch der Haut und Geschlechtskrankheiten, Jena, Gustav Fischer, 1920.

Tumors.—The Danlos syndrome is not complete without the presence of violaceous pseudotumors composed of blood elements and produced by trauma. In Hallopeau and de Lépinay's case the lesions were present on the elbows and knees, and an icteric tint caused them to diagnose the tumors erroneously as pseudodiabetic xanthoma. The clinical observations of Danlos and the biopsy examinations of Pautrier finally settled the diagnosis as traumatic pseudotumors of cutis laxa. Schulmann's case was also typical. The lesions occurred on the elbows, arms, fingers and feet as raised, soft, violaceous "tumors" with irregular surfaces not unlike raisins, and molluscoid. The nodules were also present over the achilles tendon, but not connected with it. In Margarot's patient the latter site was also involved as well as the feet, but the lesions were more fibromatous. The buttocks, knees and shoulders also presented growths. The only evidence of development of true tumor in Martin's case was a solitary, painless, fibromatous nodule in an atrophic scar over the left elbow.

In my case there was generalized lipomatosis, the lesions being small and demonstrable only by palpating the skin. There was no deformity of the overlying surfaces. On the forearms, legs and posterior parts of the thighs was a linear distribution which conformed to the theory of involvement of the nerves in Recklinghausen's disease. There was also a large, soft, violaceous pseudotumor of Danlos over the olecranon process of the right radius about the size of a brazil-nut which followed trauma. This pseudotumor began to disappear in four days, following decompression with a tight dressing.

PATHOLOGIC PROCESS

Some confusion exists among observers in the conclusions to be derived from a study of the sections of cutis laxa. The important changes are found in the corium. Williams [20] found the elastic tissue normal, with a thinning out and a rarefaction of the collagenous fibers. Reyn's [21] cases were marked by changes in the collagenous tissue characterized by hypertrophy and spinal torsion. There was a tendency to hemorrhage in the skin and subcutaneous tissue. This might have been produced by trauma in removing the section for examination. On the other hand, Martin found hypertrophy of the elastic tissue network and thickening of the collagenous bundles with clumps of fibrous tissue cells scattered in various areas. The arrectores muscles were larger than normal and had a tendency to be parallel to the surface of the skin. There was moderate vascular dilatation. Spinal torsion of the vessels and nerves has been described. Bielschowsky reported pigmentary deposits in the corium and neuromas in the cutaneous nerve endings, which suggest a relationship to Recklinghausen's disease.

20. Williams, A. W.: Cutis laxa, Monatschr. f. prakt. Dermat. **14**:490, 1892.
21. Reyn, A.: Cutis Laxa: Two Cases, Hospitalstid. **76**:961 (Sept. 28) 1933.

The entire section of skin was much thinner than normal, with marked diminution of subcutaneous or supporting tissue. The malpighian layer was thinned out, with poor development of the basal layer. The papillae were small and reduced in number owing to a flattening of the germinal layer.

Pautrier's [4] description of the histology of changes of the tumors in Danlos' case is classic, and is recorded here, as biopsies were not done in Margarot's case and were not permitted in my patient.

Epidermis: The horny layer, rather thin, is represented by one or two cornified layers in the process of exfoliation.

The granular layer is, in general, thickened and formed at certain points by three or four rows of cells loaded with granules of eleidin. They reach at other points the thickness of six or seven cellular rows.

The mucous body, markedly hyperacanthotic, forms voluminous interpapillary buds. These, thickset and rather elongated, surrounded the high papillae. The basal layer is extremely regular and perfectly formed.

At the level of a certain number of large interpapillary buds are found, between the basal layer and the subjacent dermis, a sort of clear cavity, extremely narrow, which surrounds the foot of these interpapillary buds. When one examines these points under high power magnification one sees that these clefts are limited in places by a type of endothelial cell, very flat and elongated and so well marked that one may wonder if these are not lymphatic spaces.

Dermis: In the superficial region of the dermis the dominating thing outside the lymphatic clefts just described is the existence of numerous dilatations of the blood and lymphatic capillaries. Sectioned nearly always transversely, the first, of small caliber, are filled with red corpuscles and are very close to each other. Their endothelium does not appear to present any appreciable pathologic process.

The same dilatations are found again in the middle part of the dermis, but at this level they are located on more important vessels. The latter, sectioned now longitudinally, now transversely, form large gaping cavities filled with red corpuscles, coming at certain points almost in contact with each other, thus forming truly angiomatous tissue. The endothelium does not always seem to be altered.

At one end of the section, just underneath the papillary body, that is, in the superficial corium, is a voluminous vein with a rather thick wall, the like of which is not commonly found in this region; like the other vessels, it is filled with red corpuscles. The lymphatic vessels are likewise more numerous than normal and markedly dilated.

Along the circumference of all these vascular cavities is a rather discrete infiltration of cellular elements. They form little heaps composed in large part of cells of the type of fixed cells. Outside these elements are found little cells formed almost uniquely by a rounded nucleus, strongly basophilic, surrounded by a thin shell of protoplasm, a type of lymphocyte; finally, at several points, several plasma cells are found.

In the interval between these are not very dense, little, cellular groupings, disseminated around the vessels. The fibers of collagen present nothing abnormal, nor is there anything singular about the elastic network of the dermis, which is normal.

In conclusion the lesions may be said to be due to the presence of this angiomatous tissue of the middle dermis.

CONCLUSIONS

1. A case of cutis laxa presenting the Danlos syndrome of laxity of the joints, scarring following trauma and pseudotumors is reported.

2. The association of congenital lipomatosis is unique.

3. Disturbances in the tissue of this nature fall into the broad group of Recklinghausen's disease.

DERMATOFIBROSIS LENTICULARIS DISSEMINATA AND OSTEOPOIKILOSIS

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The purpose of this report is to call attention to an interesting lesion of the skin which occurs in association with characteristic lesions of the bones. Only a few cases of this disease have been reported, but the lesions are so inconspicuous that it is possible that many cases have been overlooked.

OSTEOPOIKILOSIS

In 1915 Albers-Schoenberg [1] described the case of a man, 22 years old, in whom roentgen examination revealed numerous minute lesions in all bones except the skull, spine, scapula, patella and clavicle. They were located chiefly in the epiphyses, though isolated lesions were found in the diaphyses. The lesions appeared as minute oval areas of condensation, usually with the long axis in the direction of the long axis of the bone. Their size varied from that of the head of a pin to that of a pea. They were sometimes so numerous as to make the bone look spotted in the roentgenogram. The patient complained of rheumatic pains in one shoulder and foot. Other factors which might cause the involvement of the joints independently of the existing disease of bone could not be found. No other lesions were found except some questionable exostosis. Albers-Schoenberg gave the disease the name "osteopoikilie." The following year Ledoux-Lebard, Chabaneix and Dessane [2] described a case which seems to have been similar except that there were no symptoms. Since that time thirty-three additional cases presenting the same characteristic x-ray picture, with or without pains in the bones and joints, and occasionally associated with other lesions which will be mentioned later, have been described. Wachtel [3] called the disease osteopathia condensans disseminata.

The lesions of the bones in the majority of these cases have been strikingly similar in character and distribution. However, the patient described by Guillan and Mollaret [4] showed typical lenticular condensa-

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1. Albers-Schoenberg: Fortschr. a. d. Geb. d. Röntgenstrahlen **23**:174, 1915.
2. Ledoux-Lebard; Chabaneix, and Dessane: J. de radiol. et d'électrol. **2**:133, 1916.
3. Wachtel, H.: Fortschr. a. d. Geb. d. Röntgenstrahlen **27**:625, 1921.
4. Guillan, G., and Mollaret, P.: Bull. et mém. Soc. méd. d. hôp. de Paris **54**:214 (Feb. 24) 1930.

tions limited to the bones of the left hand. Bistolfi [5] is the only one who reported spots in the occiput, while in all the other cases the skull was found free from changes. Vorhoeve [6] reported three cases of slightly different character, all appearing in the same family. The father showed only the spots of condensation, described by Albers-Schoenberg.[1] His two children showed streaks of condensation extending from the epiphyseal lines to varying distances in the diaphysis, but none of the oval spots. This appearance led Vorhoeve to conclude that the lesions

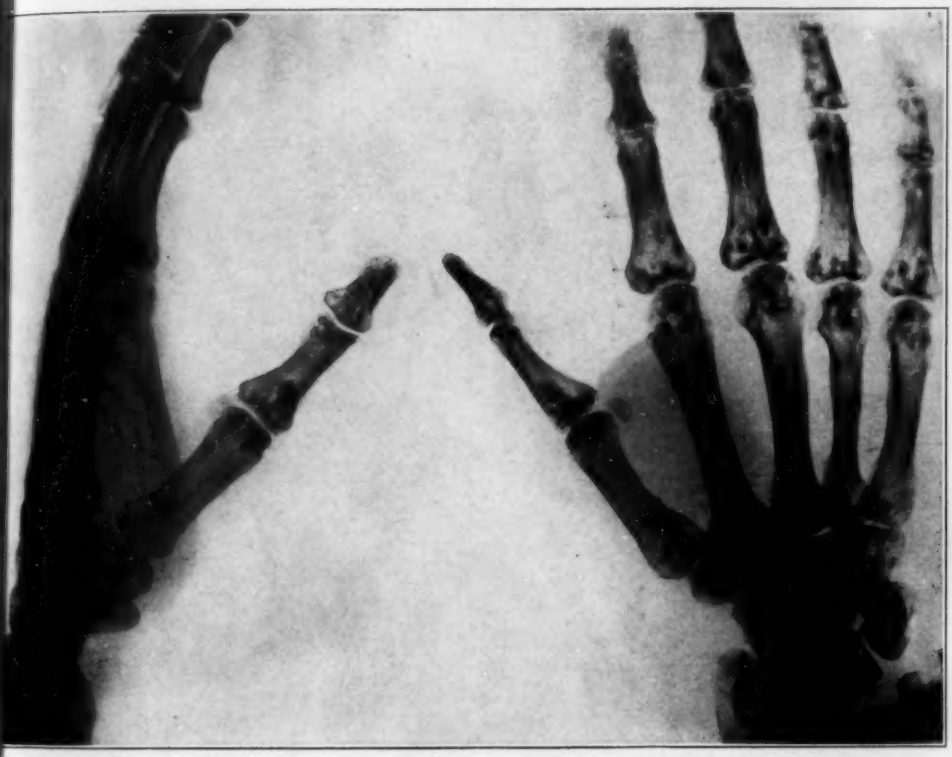

Fig. 1.—Typical case of osteopoikilosis (courtesy of Dr. W. S. Newcomet, Philadelphia).

are connected one with another, and that they originate in the cartilage. Similar streaks, associated with the oval lesions, were observed by Moreau,[7] Schele [8] and Windholz.[9] Mascherpa [10] found only streaks in

5. Bistolfi: Radiol. med. **14**:1024, 1927.
6. Vorhoeve, N.: Acta radiol. **3**:407, 1924.
7. Moreau, L.: J. de radiol. et d'électrol. **3**:318, 1918.
8. Schele: Acta radiol. **1**:536, 1922.
9. Windholz, F.: Wien. klin. Wchnschr. **44**:1611 (Dec. 11) 1931; Fortschr. a. d. Geb. d. Röntgenstrahlen **45**:566 (May) 1932.
10. Mascherpa, F.: Radiol. med. **18**:1014 (Aug.) 1931.

his cases, but he did not confirm Vorhoeve's theory of the enchondral origin.

The first histologic examination was reported by Schmorl,[11] in 1931, who performed an autopsy on a youth of 18 years. Beside showing the characteristic picture of osteopoikilosis, he had osteomyelitis, amyloidosis and pyonephrosis following lithiasis. Schmorl described the lesions as small osteoma-like formations, interspersed between the fine trabeculae

Fig. 2.—Typical case of osteopoikilosis (courtesy of Dr. W. S. Newcomet, Philadelphia).

of the spongiosa. The lesions in the diaphysis were grayish, and were found where the trabeculae of the spongiosa are attached to the osseous cortex. They consisted of spongiosa substance with thickened trabeculae. There was no evidence of enchondral origin. These osteoma-like formations coincide with the histologic report by Windholz of a "Kompaktainsel." Thus Albers-Schoenberg's theory that the changes in bone

11. Schmorl, G.: Fortschr. a. d. Geb. d. Röntgenstrahlen **44**:1, 1931.

Fig. 3.—Dermatofibrosis lenticularis disseminata (case of Buschke and Ollendorff Curth).

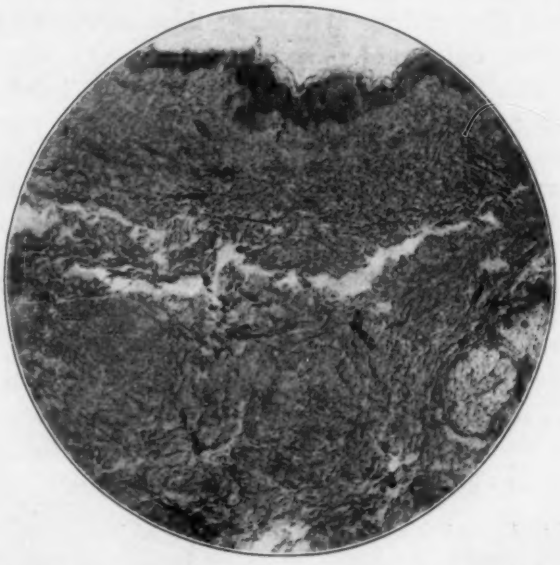

Fig. 4.—Histologic appearance of cutaneous lesion of dermatofibrosis lenticularis disseminata (case of Buschke and Ollendorff Curth).

in osteopoikilosis were of the nature of the so-called "Kompaktainsel" finds other support.

DERMATOFIBROSIS LENTICULARIS DISSEMINATA

In 1928 Buschke and I [12] described the case of a woman of 41 years, who presented papular lesions symmetrically distributed over the upper part of the back and arms, the lumbar region, the buttocks and the thighs. The lesions were slightly raised, the size of a pea, oval or nearly round and of the same color as the surrounding skin. They were firm, and could be felt better than seen. They were closely agminated. It is remarkable that the skin of the face was not involved, particularly in consideration of the fact that the bones of the skull are practically never affected. In addition to the cutaneous lesions she showed the characteristic picture of osteopoikilosis, as described by Albers-Schoenberg. The patient was infantile and was poorly nourished. She had numerous keloids and striae and a capillary nevus in the region of the shoulder. She complained of severe pain in the shoulders and the upper part of the arms and had various gastro-intestinal disturbances. There had been no symptoms attributable to her cutaneous lesions.

Histologic examination of a typical lesion of the skin showed a focus of fibromatous thickening of the cutis without destruction of the elastic fibers. There was no sharp line of demarcation from the normal cutis. There was no evidence of inflammatory reaction, and, in fact, nothing abnormal was seen except the increase in the number of normal-appearing bundles of collagen.

Three similar cases have been reported by Windholz [9] and one by Šváb,[13] in each of which the lesions of osteopoikilosis were presented.

In addition, Pokorny and Pokorny,[14] in 1929, reported under the name of dermatofibrosis lenticularis disseminata three cases occurring in one family. They showed various types of lesions, some papular, some level with the skin and others which consisted of atrophy and slightly pigmented scars. The papules changed into pigmented and atrophic spots in from three to seven years. No such evidence of atrophy and pigmentation was seen in any of the other five cases of dermatofibrosis lenticularis disseminata reported. It would seem that the cases of the Pokornys should not be grouped under the condition here described, because they were probably a form of scleroderma. It should be noted that the patients showed no evidence of osteopoikilosis.

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12. Buschke, A., and Ollendorff, H.: Dermat. Wchnschr. **86**:257 (Feb. 25) 1928.

13. Šváb, V.: J. de radiol. et d'électrol. **16**:405 (Sept.) 1932; Časop. lék. česk. **71**:743 (June 10) 1932.

14. Pokorny, A., and Pokorny, L.: Dermat. Wchnschr. **88**:157 (Feb. 2) 1929.

Case	Author	Year	Age	Sex	Other Cases in Family	Osteopoikilosis	Location in bone	Dermatofibrosis Lenticularis Disseminata	Pains in Bones and Joints	Associated Symptoms and Lesions
1	Albers-Schoenberg [1]	1915	22	M	—*	+	All except skull, spine, scapulas, patellas and clavicles	—	+	Questionable exostosis
2	Ledoux-Lebard, Chabaneix and Dessane [2]	1916	28	M	—	+	All except skull, spine and ribs...	—	—	
3	Moreau [7]	1918	31	M	—	+	All except skull, spine and ribs...	—	—	Supernumerary rib; tuberculosis of spine; sacrolumbar ankylosis
4	Wachtel [3]	1921	23	M	—	+	All except skull, spine, scapulas, clavicles	—	+	Arthritis deformans
5	Schele [8]	1922	34	M	—	+	All except skull	—	0	
6	Richarz: Fortschr. a. d. Geb. d. Röntgenstrahlen **28**: 87, 1921	1922	31	F	—	+	All except skull, spine, scapulas and patellas	—	0	
7	Vorhoeve [6]	1924	?	M	+	+	All except skull	0	—	
8	Vorhoeve [6]	1924	14	M	+	+?	All except skull	0	+	Supernumerary vertebra; testicles undescended
9	Vorhoeve [6]	1924	10	F	+	+?	All except skull	0	+	
10	Steenhuis [15]	1926	13	F	—	+	Not individually mentioned	—	—	Peritoneal fibrous nodules
11†	van Dorp-Beucker and Andreae [17]	1928	17	F	?	+	Not individually mentioned	—	—	Tuberculous peritonitis
12	Bistolfi [5]	1927	21	M	—	+	All except skull and ribs; occiput	—	—	
13	Buschke and Ollendorff [12]	1928	41	F	—	+	All except skull, ribs and spine...	+	+	Keloids; striae; nevus; infantilism; gastritis
14	Amundsen: Acta radiol. **11**: 120, 1929	1929	30	F	—	+	All except skull, spine, ribs and clavicles	—	—	Abdominal pain
15	Gluch: Röntgenpraxis **1**: 505, 1930	1929	19	F	—	+	All except skull	—	—	Anemia
16	Newcomet [18]	1929	50	M	—	+	All except skull	—	—	
17	Kahlstorf: Röntgenpraxis **2**: 721, 1930	1930	26	M	—	+	All except skull, ribs and spine...	—	—	
18	Awalischwili: Röntgenpraxis **2**: 831, 1930	1930	24	M	0‡	+	Pelvis and lower extremities	—	+	Anemia
19	Koenig: Fortschr. a. d. Geb. d. Röntgenstrahlen **42**: 406, 1930	1930	..	M	—	+	All except skull	—	—	
20	Guillan and Mollaret [4]	1930	32	M	—	+	Only left hand	—	0	Achondroplastic dwarf: supernumerary nipple; vitiligo
21	Schmorl [11]	1931	18	M	—	+	All except skull, spine and clavicle	—	—	Osteomyelitis; amyloidosis; nephrolithiasis
22	Reiser and Laufer: Fortschr. a. d. Geb. d. Röntgenstrahlen **43**: 808, 1931	1931	54	F	—	+	Only extremities	—	+§	Gastric ulcer
23	Wilcox: Am. J. Roentgenol. **27**: 580, 1931	1931	52	M	+	+	All except skull and ribs	—	—	
24	Wilcox: ibid.	1931	21	M	+‖	+	All except skull and ribs	—	—	Abdominal pain
25	Haack: Röntgenpraxis **3**: 611, 1931	1931	26	M	—	+	All except skull, ribs, shoulder, sternum and vertebrae	—	0	
26	Volicer [16]	1931	16	M	—	+	Typical bones involved	—	+	
27	Mascherpa [10]	1931	20	M	+	+?	All except skull and ribs	—	—	
28	Mascherpa [10]	1931	18	M	+	+?	All except skull and ribs	—	—	
29	Mascherpa [10]	1931	10	F	+	+?	All except skull and ribs	—	—	
30	Windholz [9]	1932	46	M	+	+	Typical bones involved	+	+	Neuropathy; gastritis
31	Windholz [9]	1932	10	F	+¶	+	Typical bones involved	+	+	Sexus anceps; scar keloid
32	Windholz [9]	1932	19	M	—	+	Typical bones involved	+	0	Malformation of one tooth
33	Šváb [13]	1932	54	M	+	+	All except skull and spine	+	0	Diabetes; striae atrophicae
34	Šváb [13]	1932	28	M	+	+	All except skull	0	0	
35	Šváb [13]	1932	27	M	+	+	All except skull	0	0	

* Plus sign means present; naught, none, and minus sign, not reported.
† This case is apparently identical with case 10.
‡ Seven members were normal, two were not examined.
§ Transitory rheumatic pain was noted in one hand.
‖ One brother and one sister were normal.
¶ One brother was normal

The lesions of dermatofibrosis lenticularis disseminata are so inconspicuous that it is possible that they have been overlooked in some of the reported cases of osteopoikilosis. However, they were carefully looked for and not found in two of Šváb's cases [13] and in two other cases (father and son) which I recently observed, so that there can be no doubt that the lesions of bone can occur in the absence of cutaneous lesions. In all the few reported cases of dermatofibrosis lenticularis disseminata, osteopoikilosis was present, but this does not warrant the conclusion that the lesions of the skin cannot occur in the absence of lesions of the bone.

OTHER ASSOCIATED LESIONS

Steenhuis,[15] in 1926, described a patient who complained of severe abdominal pains. A laparotomy was performed, and small white lesions the size of a pea were found scattered over the peritoneal surface. From Steenhuis' description these would seem grossly to resemble the lesions which I have observed in the skin. Histologically they showed some resemblance to tuberculosis, but the resemblance was not thought sufficient to warrant that diagnosis (Driessen). It is of interest in this connection that in many of the reported cases of osteopoikilosis unexplained abdominal pain was reported among the symptoms.

In a number of other cases abnormalities in development were reported. My patient was mentally defective. The patient of Guillan and Mollaret [4] was an achondroplastic dwarf. The father of the familial group reported by Windholz [9] was neuropathic and the daughter suffered from sexus anceps. His third patient had malformation of one tooth. One of Vorhoeve's [6] patients had a supernumerary vertebra and undescended testicles.

Other cutaneous manifestations seem to be combined with the dermatofibrosis lenticularis disseminata: striae (in my patient and Šváb's), keloids (in my patient and in one of Windholz') and nevi (in my patient).

ETIOLOGY

Nothing definite is known as to the etiology of the lesions. As the lesions of neither bone nor skin cause definite symptoms, it is impossible to determine from the histories the age at which they originated. In discussing the report of Steenhuis, Heilborn stated that he had seen similar lesions in a 4 month old fetus, and Keyser stated that he had seen them in the spine of a child a few days old. These cases have never been reported in detail and may not have been true osteopoikilosis. They suggest, however, that the lesions may be of congenital origin. The frequency of the occurrence of several cases in a family would

15. Steenhuis, D. J.: Acta radiol. **5**:373, 1926.

support this view; but there are families in which only one member, or several members, but not all are affected. Thus it must be a non-dominant hereditary disease.

Little is known as to the progression or involution of the lesions. Volicer [16] noted an increase in the number of the lesions of bone on a second examination of his patient. Van Dorp-Beucker and Andreae [17] on second examination reported a decrease in the lesions, but a recent examination failed to show a "relative" decrease. Newcomet [18] reexamined his patient after four years and could see no change.

It is of interest that all lesions involve the mesenchymal tissue; it would seem probable that the lesions represent a hereditary localized malformation of this tissue. There is nothing in the previous history of these patients which seems to throw a light on the etiology. No infectious or constitutional disease is reported with special frequency. Smallpox and chickenpox occurred in some of the patients with osseous lesions, but in none who presented cutaneous lesions. The histologic appearance would seem to differentiate lesions described here from scars of either of these eruptive fevers.

There is as yet no evidence of any endocrine change as the cause of this disease.

Brünauer [19] classified dermatofibrosis lenticularis disseminata with the sclerodermas. The papular character of the lesion and the apparent congenital origin of the disease would seem to make such classification illogical.

DIAGNOSIS

In the diagnosis of dermatofibrosis lenticularis disseminata the differentiation from scars, keloids and morphea guttata must be considered. The lesions are invariably raised. The skin shows no variation from normal color. The uniformity of the lesions and the absence of evidence of evolution is striking. Their definitely papular character and normal pigmentation differentiates them from morphea or white-spot disease.

The presence of other cutaneous manifestations often associated with osteopoikilosis should lead to the suspicion of its presence. In patients presenting striae, keloids and nevi, alone or in combination, a careful search should be made for the lenticular lesions described here, and roentgen examination should be made of the more commonly involved bones, such as those in the hands.

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16. Volicer, L.: Časop. lék. češk. **70**:1021 (July 17) 1931.

17. van Dorp-Beucker and Andreae, D.: Nederl. tijdschr. v. geneesk. **72**:1012, 1928.

18. Newcomet, W. S.: Am. J. Roentgenol. **22**:460 (Nov.) 1929.

19. Brünauer, S. R., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 8, p. 772.

CONCLUSIONS

Osteopoikilosis and dermatofibrosis lenticularis disseminata apparently represent two manifestations in different organs of a similar lesion of the connective tissue. In one instance lesions of the same type occurred in the peritoneum. The disease is probably a hereditary anomaly.

NOTE.—Since this paper was submitted for publication, a number of reports on osteopoikilosis have been published. Kadruka and Hirleman,[20] Arthur Bloom [21] and Kudrjavceva saw involvement of several members of a family. Two Russian reports [22] were not available. Hugh Jeter and C. L. MacGehee [23] and van Pee [24] have each reported cases. None of these reports mention dermatoxofibrosis lenticularis disseminata.

More important than the enumeration of these cases seems to be a new discussion of the relationship between osteopoikilosis and scleroderma. Von Bernuth [25] described the occurrence of scleroderma and osteopoikilosis in a child. Scleroderma was present at the age of 7 months and was rapidly progressive. At the age of 6 years osteopoikilosis was discovered, but retrospectively this diagnosis was already suggested on the roentgenogram taken at the age of 7 months. Delherm, Morel, Kahn and Coupul [26] previously reported a case of scleroderma which showed minute opacities in the phalanges. These they concluded were not true osteopoikilosis, but deposits of calcium similar to those seen in the subcutaneous tissues in scleroderma. In von Bernuth's case, on the other hand, there seems little question as to the diagnosis of osteopoikilosis, but there is no proof that its occurrence in a case of scleroderma was more than a coincidence.

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20. Kadruka and Hirleman: Rev. d'orthop. **20**:29 (Jan.) 1933.
21. Bloom, A.: Am. J. Surg. **22**:239 (Nov.) 1933.
22. Kudrjavceva: Šovrem. Chir. **5**:33, 1930. Sitenko: Ortop. i travmatol. 1930, cited by Holst: Roentgenpraxis **4**:52, 1932.
23. Jeter, H., and MacGehee, C. L.: J. Bone & Joint Surg. **15**:990 (Oct.) 1933.
24. van Pee: Liège méd. **24**:937, 1931.
25. Von Bermuth: Ztschr. f. Kinderh. **54**:103, 1932.
26. Delherm, Morel; Kahn, and Coupril: Bull. soc. radiol. med. **13**:118, 1925.

NEUROSYPHILID OF UNNA AS A MANIFESTATION OF CONGENITAL SYPHILIS

FORME FRUSTE OF LATE CUTANEOUS SYPHILIS

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The rare cutaneous manifestation of late syphilis first accurately described by Fournier [1] under the name of "érythème circiné tertiaire," has been reported in about fifty cases of acquired syphilis.

F. Combes [2] recently reported the condition in acquired syphilis, with histologic observations and a full review of the literature. Review of the available literature reveals no report of this type of eruption occurring as a manifestation of congenital syphilis. The eruption, as emphasized by Fournier, is a late (tertiary) manifestation, and has no relation to the early annular macular and annular papular eruptions not infrequently observed in recently acquired syphilis.

Unna [3] studied the condition extensively, and this rare eruption of late syphilis is usually known as the neurosyphilid of Unna. The name, neurosyphilid, is probably inappropriate, as evidence (clinical or serologic) of syphilis of the central nervous system is often lacking.

The lesions of érythème circiné tertiaire, or neurosyphilid of Unna, appear in full bloom as erythematous, irregular, annular macules or macular papules. Gyrate and serpiginous configurations also occur. The eruption is limited to the trunk and extremities. There are no subjective symptoms. The lesions persist for long periods, with no change in number, size or configuration. The entire absence of any tendency to ulceration is a striking distinction from the usual cutaneous eruptions of late syphilis.

The lesions are usually annular macules; however, papular types have been described by numerous observers. The color is pale pink. The intensification of the color by friction and heat is a striking feature, as has been emphasized by Unna. Variation in color was noticed by the patient in our case.

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1. Fournier, A.: Roséoles syphilitiques à récidives multiples, Ann. de dermat. et syph. **7**:1141, 1896.

2. Combes, F.: The Annular Macular Syphilid (Neurosyphilid, Unna), Arch. Dermat. & Syph. **25**:906 (May) 1932.

3. Unna, P.: Histopathology of the Diseases of the Skin, translated by Norman Walker, Edinburgh, W. F. Clay, 1896, p. 124.

REPORT OF A CASE

C. S., a white woman, aged 20, was first examined at the West Side Health Center in January 1934. According to the history, the lesions had been present for six weeks, and had not changed since she had first noticed them.

The eruption was limited to the trunk and extremities. There were approximately fifty lesions. They were more profuse in the lumbar and posterior pelvic regions than elsewhere. The eruption consisted of grouped erythematous, macular papules the size of BB shot, forming irregular annular and gyrate configurations from 1.5 to 5 cm. in the longest diameter. Many of the papules seemed to be centered around a hair follicle.

The application of hot moist towels and friction intensified the color of the lesions and made the papular elements more prominent. On pressure the lesions disappeared entirely, except for a faint yellowish tinge.

Fig. 1.—Lesions as they appeared over the buttocks.

Two days following the intramuscular injection of a soluble bismuth citrate preparation the lesions were intensified in color; however, they started to fade gradually one week after antisyphilitic treatment with bismuth was instituted, and at the end of six weeks, under further bismuth therapy, disappeared entirely.

The first four Wassermann and Kahn tests of the blood gave negative results, possibly owing to the fact that the patient had been drinking heavily at the time the tests were taken. On the fifth test separate specimens of blood were sent to two laboratories. One reported both the Kahn and the Wassermann reactions positive, the other a Wassermann reaction of 4 plus. The spinal fluid gave a negative reaction to all tests. There was no clinical evidence of cerebrospinal syphilis. The only clinical evidence of congenital syphilis was a high arched palate, the eruption and positive serologic changes. However, the fact that the eruption occurs years after infection with syphilis, and the following parental and personal history gave conclusive evidence that the patient had congenital syphilitis.

Her mother had advanced tabes dorsalis of several years' duration. According to her history, this was due to a syphilitic infection acquired while she was preg-

nant with the patient. At that time a rash appeared on the mother which was pronounced syphilitic by her physician, who gave her antisyphilitic treatment by mouth. Our patient was apparently normal at birth. There were no other children, but several miscarriages.

The father, an inmate of a state hospital, had the tabetic form of dementia paralytica. His syphilitic infection was said to have been contracted prior to the birth of our patient.

The patient's personal history revealed that she had had the usual diseases of childhood, but had never been seriously ill. There was no history of acquired syphilis.

The patient was married in 1930 and lived with her husband for one year. There were no pregnancies. No history of syphilis in the husband was obtainable. The patient admitted that she used alcoholic stimulants to excess at times.

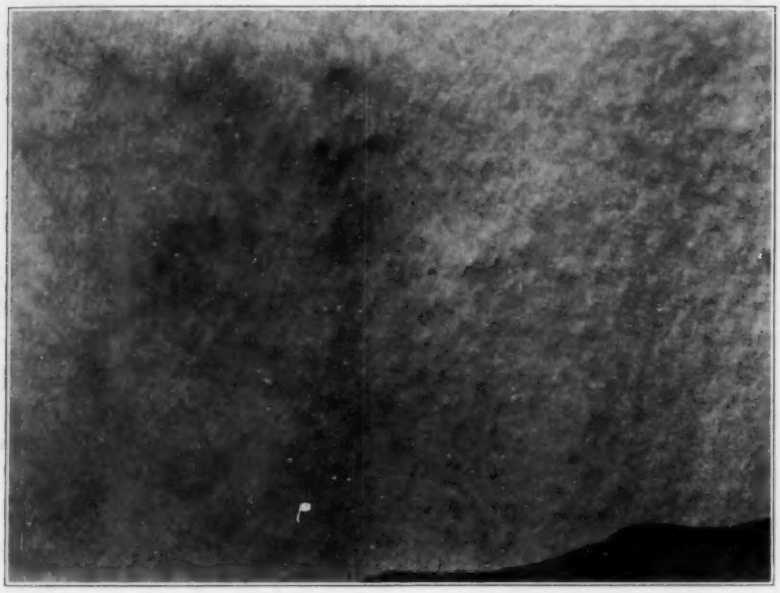

Fig. 2.—Close up of a lesion.

For histologic examination a section was removed from one of the lesions on the left thigh, and stained with hematoxylin and eosin. There were no marked changes apparent in the epidermis. There was a moderate perivascular infiltration around the vessels of the cutis which was more pronounced in the upper half of the cutis.

High power microscopic examination revealed that the perivascular infiltrate in the cutis was composed of numerous plasma and round cells. The vessels of the cutis showed evidence of endothelial proliferation. This was especially marked in the arterial capillaries, and had in some instances progressed almost to obliteration; however, none of the vessels showed complete obliteration or thrombosis, as is commonly seen in the usual types of late syphilis of the skin. The small veins were less affected than the small arteries.

The perivascular infiltrate and endothelial proliferation of the small vessels were the only apparent important histologic changes in the cutis.

COMMENT

Approximately fifty cases of so-called neurosyphilid of Unna have been reported in the literature. The cases previously reported have been in patients with acquired syphilis. Our case proves that the condition may also occur as a manifestation of congenital syphilis.

There seems to be no essential difference in the clinical or histologic features from those found when the eruption occurs in acquired syphilis.

For the following reasons, we believe that the neurosyphilid of Unna may be considered an abortive type of late granulomatous syphilis of the skin.

The fact that the lesions differ in certain respects, clinically and histologically, from the usual late syphilitic cutaneous eruptions is due probably to a general or local immunologic difference, which in some unknown way prevents the complete formation of the usual clinical and histologic features of late syphilis.

Clinically, this unusual late type of syphilitic eruption has many points in common with the usual late papular tuberculous lesions.

The onset, years after infection, and the fact that the lesions are composed of grouped macules or macular papules which show a marked tendency to form annular, circinate, serpiginous and gyrate rings are prominent features, shared with the more usual types of late syphilis of the skin.

The small number of lesions in comparison to those of early eruptive syphilis is in conformity with late cutaneous involvement.

The tendency of the lesions to persist for long periods of time approximates the condition of late syphilis.

However, the tendency of the lesions to remain unchanged is a condition, as a rule, not found in tertiary cutaneous lesions. The frequent occurrence of concomitant typical granulomatous forms of late syphilitic eruptions is one of the strongest arguments for the theory that the neurosyphilid of Unna is merely a forme fruste of the late papular tuberculous syphilid.

Histologically, one may consider the neurosyphilid of Unna a syphilitic lesion which falls short of the granulation tissue stage of late syphilis. Aside from the absence of granulation tissue it closely approaches, in many respects, the histologic features of late syphilis of the skin.

Thus, there is the typical coat sleeve type of infiltrate, with numerous plasma and round cells. The endothelial proliferation, in many respects, is similar to that seen in granulomatous syphilis; however, the degree of involvement is less than that seen in late syphilis, as complete obliteration or thrombosis of the vessels with necrosis of the surrounding tissue does not occur.

The clinical and histologic features are characteristic and, taken together, make the differentiation from chronic urticaria, erythema perstans, lichen scrofulosus, pityriasis rosea, seborrhea corporis and other dermatoses not difficult.

The lesions have often been reported as resistant to antisyphilitic treatment. However, in our case the intensification (Herxheimer's reaction) after the first injection of soluble bismuth and the disappearance under continued bismuth therapy were clearly indicative of the syphilitic nature of the eruption.

ACNEFORM RESPONSES TO PATCH TESTS

FOLLICULAR AND PAPULOPUSTULAR REACTIONS TO SELECTIVELY PILOSEBACEOUS IRRITANTS

MARION B. SULZBERGER, M.D.
NEW YORK

Long established clinical and histologic observations have made it apparent that certain hematogenous dermatoses selectively affect the pilosebaceous apparatus and thus have a predominantly follicular localization.

Lichen scrofulosorum (or, more appropriately, tuberculosis lichenoides), lichen trichophyticus, acneform bromodermas, iododermas and tuberculodermas (for example, the rosacea-like tuberculid of Lewandowsky [1]) and certain eruptions due to arsphenamine and other drugs, appearing as a lichen spinulosus (Stauffer [2]), are examples of the many dermatoses in which a hematogenously distributed agent shows a certain predilection for affecting the follicles of the skin.

Struck by this, many investigators have sought to explain this selectivity. J. Jadassohn [3] has repeatedly called attention to the fact that the anatomic and functional characteristics of the blood vessels surrounding the pilosebaceous invaginations were peculiarly conducive to a concentration of hematogenous substances, and particularly to a deposit of hematogenously distributed micro-organisms at these points.

In the case of iododermas and bromodermas, it has been pointed out that the respective halogens are excreted with the sebum and that this fact accounted, at least in part, for their concentration in the follicles and their tendency to produce follicular irritation and acneform eruptions (Stein [4]).

Certain clinical observations seemed to show that these explanations, while true as far as they went, were not entirely adequate, and that neither the follicular concentration due to peculiarities in the circulatory

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From the Department of Dermatology and Syphilology New York Post-Graduate Medical School of Columbia University, direction of Dr. George M. MacKee.

1. Lewandowsky, F.: Ueber Rosaceaähnliche Tuberkulide des Gesichtes, Cor.-Bl. f. schweiz, Aerzte **47**:1280 (Sept. 29) 1917.

2. Stauffer, H.: Leichen spinulosus als Salvarsanexanthem, Arch. f. Dermat. u. Syph. **154**:217, 1927.

3. Jadassohn, J.: Hematogenous Infectious Diseases of the Skin, Arch. Dermat. & Syph. **21**:533 (April) 1930.

4. Stein, R. O., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 13, p. 105.

conditions at the follicles nor the concentration due to excretion through the follicles entirely explained the predominantly follicular localization of the dermatoses produced by halogens and other substances. For a third halogen, chlorine gas, apparently produces follicular responses even when externally applied to the skin. And still other substances,

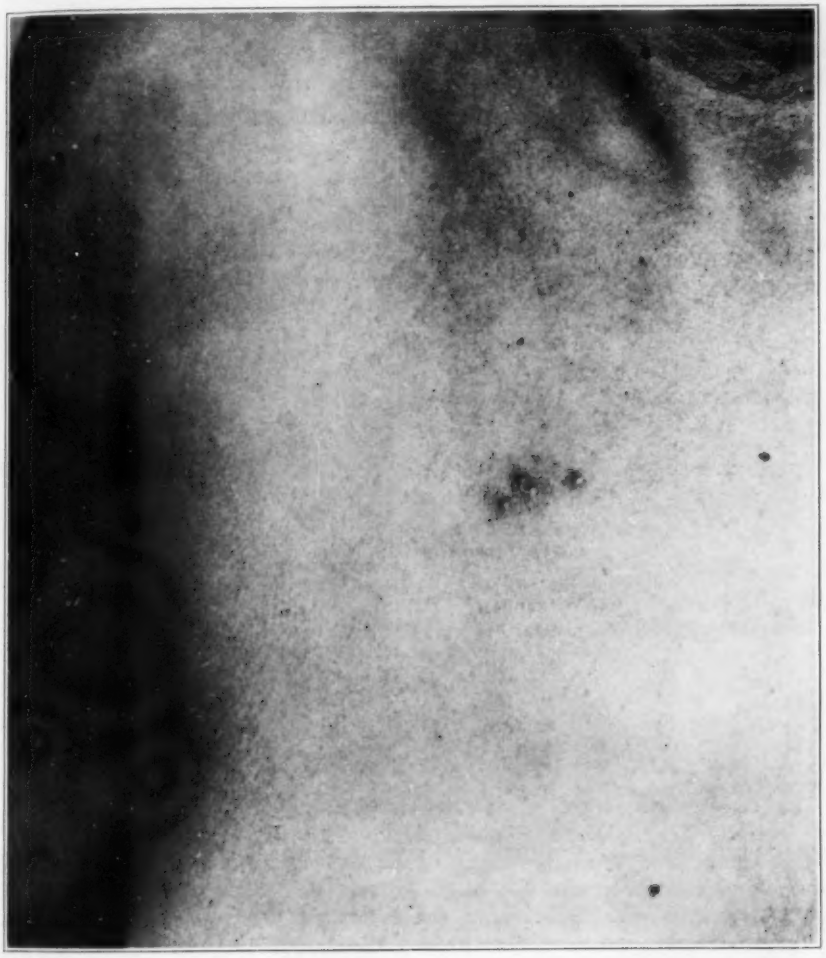

Fig. 1.—Acneform papulopustular reaction to a patch test with 25 per cent potassium iodide in hydrous wool fat on the chest of a patient with acne vulgaris of the face. Control patch tests with hydrous wool fat and many other substances gave negative results. Lesions of acne at this site persisted many weeks. The photograph was taken three weeks after the application of the test.

such as tars, greases and oils, have, when externally applied, a disposition to produce irritations in follicular sites.

It appears, therefore, that the hemodynamics peculiar to the perifollicular vessels and the effects of follicular excretion cannot be the

sole determinants of follicular localizations. Certain additional and as yet unknown factors must contribute to determine the selective action of certain substances in their disposition to cause acneform dermatoses and follicular lesions. In other words, certain substances are intrinsically and as yet inexplicably selectively pilosebaceous irritants.

The experimental confirmation of this selectivity was sought through the use of patch tests, and the results of these tests demonstrated that certain substances known to produce hematogenous follicular dermatoses may cause responses of follicular and acneform appearance, even when externally applied. Such reactions are in contrast to the usual diffuse

Fig. 2.—Acneform reaction to a patch test with old tuberculin in a patient with an acneform tuberculid. The lesions produced on the unaffected skin of this patient's arm were strikingly similar to the spontaneous papular lesions on the face. A photograph of the face of this patient may be seen in the article on rosacea-like tuberculids by MacKeen and Sulzberger (ARCH. DERMAT. & SYPH., to be published).

eczematogenous responses to patch tests. (The papulopustular and acneform reactions to patch tests are rare, and it is not to be implied that they occur with any regularity or that they are, as yet, to be interpreted as having bearing on the etiology of acneform dermatoses. For a discussion of this point, the reader is referred to the recent article on acneform eruptions.[5])

5. Sulzberger, M. B.; Rostenberg, A., Jr., and Sher, J.: Acneform Dermatoses, New York State J. Med., to be published.

Nevertheless, the following fact seems noteworthy: Among the many substances of the greatest variety which I have applied in patch tests, precisely the few substances which have the clinical disposition to cause acneform or follicular dermatoses have been by far the most frequent elicitors of acneform reactions to patch tests.

It is also to be noted that patients with acneform eruptions are those most likely to have acneform responses to patch tests.[5]

The substances which have in my experience been peculiarly disposed to elicit papulopustular reactions to patch tests were the following: (1) trichophytin, dilution 1:30; (2) old tuberculin, undiluted; (3) potassium iodide, 25 per cent, in hydrous wool fat and (4) potassium bromide, 25 per cent, in hydrous wool fat.

This predilection for causing acneform or follicular lesions cannot be attributed to peculiarities in follicular hemodynamics or to excretion with the sebum when the causal agent has been externally applied. The observation of acneform and follicular reactions to patch tests make it evident, therefore, that other as yet unknown factors contribute in the causation of selectively follicular dermatoses. The possible formation of irritants, through combination of the hematogenous or exogenous causal substances with the follicular contents (oils, fats, sterols, other lipoids and keratin), may be such a factor. On the other hand, both hematogenous and exogenous substances may become concentrated within the follicles and retained, thereby causing either primary irritation or sensitization of these sites. (J. Jadassohn has often stated his opinion that the follicles may be immunologically different from the remaining skin; i. e., hypersensitivity or immunity may, in certain cases, be localized in follicular sites.[3])

There are, of course, many other possibilities which await investigation. At present, it can be stated only that certain substances have a peculiar and intrinsic tendency to affect the pilosebaceous apparatus, even when externally applied; and that this tendency corresponds, to a certain degree, with the propensity of these same substances for hematogenously and clinically producing acneform and follicular eruptions in predisposed persons.

Clinical Notes

A CENTERING AND MEASURING DEVICE FOR ROENTGEN THERAPY

HARRY L. FRIEDMAN, M.D., DENVER

The adapter described here fits on the tube holder as does a therapy cone used to confine the rays to small areas. It is a steel plate, through the center of which there fits a telescope arrangement made of a brass sleeve and a steel shaft graduated in inches or centimeters. At the end of the shaft an ebonite knob is attached.

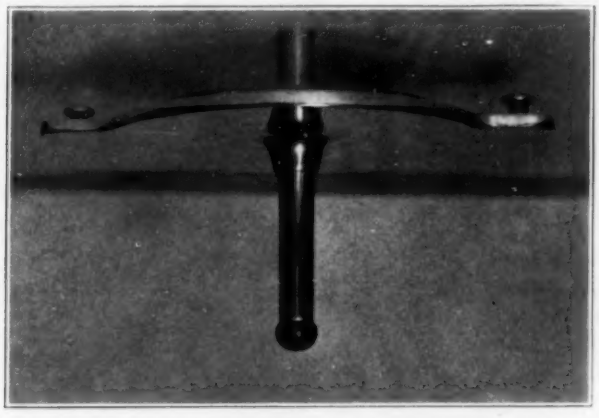

Fig. 1.—Shaft completely hidden within sleeve.

A tension spring is placed within the shaft to hold the graduated bar within any set point in the sleeve. The entire adapter, except the knob, is nickel or chrome plated. The brass sleeve can be made so that when the shaft is entirely within the sleeve, it will measure 8 inches (20.3 cm.), or preferably a little less, from the center of the anode to the bottom of the ebonite knob. If one wishes to use various distances the telescope can be made detachable by means of a screw or lock device.

If the operator wishes to treat a cutaneous lesion at a distance of 10 inches (25.4 cm.), the shaft is pulled out to the 10 mark and the tube holder lowered until the ebonite knob touches the center of the lesion. The tube holder is then fixed tightly in this position, the shaft is pushed back into its sleeve, the adapter removed and the treatment given. If one is using an 8 inch distance the sleeve must not measure more than 7½ inches (19 cm.) from the center of the anode

to the bottom of the ebonite knob with the shaft completely hidden. Otherwise the adapter will not be easily removable before giving the treatment. In such a case a figure 8 should be substituted for figure 9 on my shaft (fig. 2).

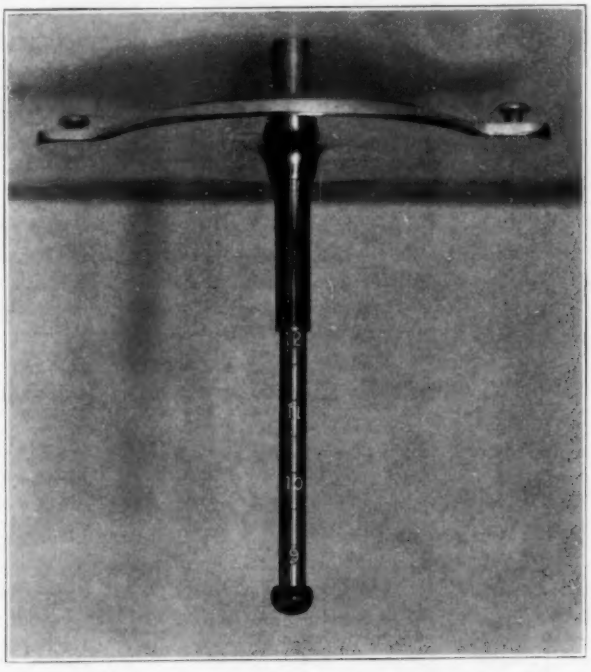

Fig. 2.—Shaft completely drawn out.

When not in use the adapter should be placed back in the diaphragm of the tube holder. The adapter can also be modified to fit the MacKee tube stand.

This device insures accuracy in measuring distance, directs most of the perpendicular rays to the lesion by exact centering, cuts down the time and assures more ease in operation.

Correspondence

"ROSACEA COMPLEX AND DEMODEX FOLLICULORUM"

To the Editor:—The recent paper by Beerman and Stokes on "Rosacea Complex and Demodex Folliculorum," in which the authors challenge the statement that Demodex may be an important factor in the causation of rosacea prompts us to call attention to several points which the authors have ignored.

It is not our purpose to defend Demodex as a pathogenic agent. In three previous papers on the subject we presented certain observations which have now covered a period of six years. As the result of these observations, rosacea has, in our experience, been converted from a most intractable disease into one which in a high percentage of cases responds readily to local treatment alone. These observations have been of inestimable value to us in the treatment of rosacea, and we have presented them to the medical profession for what they are worth.

Beerman and Stokes failed to corroborate our findings. Several reasons may be cited for this failure:

1. Beerman and Stokes conclude that Demodex folliculorum has no etiologic relationship to rosacea because in a series of twenty-three patients with rosacea from a clinic they failed to find Demodex more frequently than in a control series.

The fallacy of this argument is as follows: Demodex occurs in the sebaceous orifices of the face in practically 100 per cent of human adults. This is a recognized fact which we conceded a priori. Our entire stress has been not on whether Demodex occurred in *more patients* with rosacea than in controls, but on the fact that it occurs in *larger numbers* in most patients who have rosacea, as compared with controls. This is a crucial point.

2. Stokes and Beerman claim to have followed our technic in the search for Demodex. "Droplets of pus, numerous comedones and superficial scrapings from the area of rosacea" constituted their material. This is certainly not the technic which we described, namely: "Usually the contents of two or three pustules are examined, or in cases in which the complaint of rough dry skin is made, some of the minute dry follicular scales are picked off and examined in the same manner," i. e., under the low power of the microscope, after having been placed on a glass slide with a drop of 40 per cent potassium hydroxide.

The point which we have repeatedly emphasized is not that Demodex can be found in cases of rosacea, but that it is easily found usually in large numbers from superficial scales. In no case were scrapings made or comedones examined (comedones in our experience are rarely found in true cases of rosacea). Obviously, if comedones are squeezed out or the surface of the skin is scraped, Demodex should be found in practically 100 per cent of the cases examined. But when a droplet of pus from a superficial vesicopustule or a dry follicular scale, which is removed without pressure or squeezing, reveals from four to five up to fifteen or sixteen organisms per low power field we regard this as highly significant, and we have not been able to demonstrate Demodex with such technic, except rarely, in cases of acne vulgaris and sycosis vulgaris, which we consider as adequate controls.

3. Beerman and Stokes again failed to follow our technic in the matter of treatment. They used 10 per cent sulphur ointment alone or in combination with 10 per cent balsam of Peru. These are not the preparations which we employed.

In our earlier cases we used the following prescription for three consecutive nights, after first thoroughly washing the area with soap and water:

	Gm. or Cc.
Betanaphthol	2
Sublimed sulphur	4
Balsam of Peru	15
Petrolatum	15

This prescription contains 5 per cent betanaphthol, more than 10 per cent sulphur and more than 40 per cent balsam of Peru.

More recently, in fact for about two years, we have employed an alkaline sulphur ointment with equally good results and with little irritation. The formula of this ointment is as follows (according to the formula of the Recipe Book of the American Pharmaceutical Association):

	Gm.
Sublimed sulphur	125
Potassium hydroxide	125
Distilled water	125

Dissolve the potassium hydroxide in the water. Add the sulphur to this liquid, heating gently till dissolved. Incorporate this yellow liquid in a mixture of the following:

	Gm.
Petrolatum	225
Wool fat (anhydrous)	225

To the mixture so obtained add the following:

	Gm.
Zinc sulphate	28
Sodium hydroxide	8
Distilled water	40
Liquid petrolatum, to make	1,000 Gm.

Add the zinc sulphate to the solution of sodium hydroxide in water; this produces zinc hydroxide. Finally, add sufficient liquid petrolatum to make the product weigh 1,000 Gm. Add 5 cc. of benzaldehyde to mask the unpleasant odor.

Our pharmacist suggests putting the zinc hydroxide on filter paper and washing with distilled water, allowing it to stand over night, then adding it to the rest of the mixture; by this means one gets a much smoother ointment and one that will not separate.

In conclusion, we should like to emphasize once more our previous views regarding the etiology of rosacea. Several causes may be operative, such as the constitutional factors stressed by Beerman and Stokes, including gastro-intestinal and nervous disorders; external causes, such as exposure to sun and wind in combination with a delicate skin, and excessive infestation with a normal human parasite, Demodex folliculorum. In our experience, Demodex is found easily and in large numbers in the majority but not in all cases of rosacea. In the cases in which it is found in abundance treatment with an ointment as above indicated results in striking clinical improvement or cure within a comparatively short time, usually a matter of days or weeks. Cases in which Demodex is not found and cases of acne vulgaris do not respond to this type of treatment. Recurrences are sometimes encountered, necessitating repetition of the treatment from time to time.

SAMUEL AYRES JR., M.D.
NELSON PAUL ANDERSON, M.D., Los Angeles.

Obituary

AUGUSTUS RAVOGLI

1851–1934

In the death of Dr. Augustus Ravogli on July 25, 1934, American dermatology has lost one of its distinguished pioneers and a lovable character. Dr. Ravogli was born in Rome, Italy, on Feb. 7, 1851, his father being an accountant in the government service and his mother a professional pianist. None of his family had been physicians. He married Miss Juliette Shindelin in 1879. They had no children.

Dr. Ravogli was educated in Rome, receiving the degree of A.M. from the Roman College in 1868 and the degree of M.D. from the University of Rome in 1873. He served as intern and substitute surgeon in several of the hospitals of Rome. In competition with seventeen other students, he won a scholarship which enabled him to pursue postgraduate studies in dermatology and venereal diseases in Vienna, Praha and Berlin (1876 to 1878).

Dr. Ravogli began the practice of medicine in Rome in 1881, and two years later came to Cincinnati, where he remained the rest of his life. His ability and special training were soon recognized, and he became lecturer in dermatology in Miami Medical College in 1882, holding this position for six years. From 1889 to 1894 he served as professor of dermatology in the Ohio Medical College, and following the merger of these institutions with the university, he became professor of dermatology and syphilis in the University of Cincinnati, serving in this capacity until 1916. For many years he was attending, and later consulting, dermatologist to the Cincinnati General Hospital.

Dr. Ravogli was elected to membership in the American Dermatological Association in 1899 and became its president in 1916-1917. He was a member of the American Medical Association, the Cincinnati Academy of Medicine, of which he was at one time first vice president, the American Urological Association, the Chicago Urological Society, the Mississippi Valley Medical Society, the German Dermatological Society and the American College of Surgeons. He was an honorary member of the Italian Dermatological Society and a corresponding member of the dermatologic societies of France and Argentina.

His writings included a book on hygiene of the skin, one on the medicolegal and sociologic aspects of syphilis and over one hundred and ten articles in American and foreign journals.

The position of consular agent for the Italian government, which he held for years, helped Dr. Ravogli to become rapidly known by his former fellow countrymen and soon by the medical profession in his city. His position among Italian Americans was also aided by the fact that he had formerly served in the Italian Army as a surgeon with the rank of major and had been made a Knight of the Italian Cross. He was a member of the Medical Reserve Corps of the United States Army, but his age precluded active service in the World War.

Dr. Ravogli's active life in teaching, writing and attending medical societies did not allow much time for social pleasures. He was much interested in Masonry, being a thirty-second degree Mason (Scottish Rite), a Knight Templar and a member of the Mystic Shrine. He allowed nothing to interfere with his devotion to his wife, who in her later years was an invalid.

The love and esteem with which Dr. Ravogli was held by his many students and friends in Cincinnati was shown by a large dinner given a few years ago in his honor. Among the many who attended were the mayor of Cincinnati and a representative of the Italian government. The special occasion of the dinner was the presentation of a portrait of Dr. Ravogli, painted by a well known artist. The following greatly merited tribute is an extract from the speech of presentation:

> All of us are here to do you honor. Some are here because of gratitude for your efficient professional ministrations. Some, who are present, venerate you as teacher, guide and mentor; some again, because they remember your wisdom in counsel. All of us have come tonight with a reason and a purpose which we have in common. It is because we love you, and loving you as we do, we wish to indulge ourselves in the great pleasure of giving expression to our feelings of devotion and esteem.

The portrait was later placed in the Cincinnati General Hospital, where it is part of the gallery of portraits of Cincinnati's distinguished physicians.

Dr. Ravogli's death followed a long and distressing illness, his funeral being held in the Immanuel Presbyterian Church, of which he was a member. He is survived by a sister and brother. His medical library was willed to the Cincinnati General Hospital, and a substantial legacy was left to the Medical Department of the University of Cincinnati.

H. F.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

THE SELF-DISINFECTING POWER OF THE SKIN. L. ARNOLD and A. BART, Am. J. Hyg. **19**:217, 1935.

Living bacteria placed on the skin rapidly disappear. They cannot be demonstrated by cultural or tinctorial methods thirty or forty minutes after contact with the skin. Attempts have been made to determine the presence of antigenic substances placed on the skin. Bacillus enteritidis and fresh egg-white placed on cutaneous surfaces and allowed to dry in the air could not be demonstrated in washings collected from such exposed surfaces. These antigens could be demonstrated in cornified epithelial scrapings mechanically removed from such exposed skin. The human skin possesses a power of destroying exogenous bacteria placed in contact with it. Desiccation is not a major factor in this mechanism of controlling the viable bacterial flora on a clean cutaneous surface. Evidence is presented to indicate that keratin may play a rôle in the removal of bacterial as well as other antigens from human skin.

AUTHORS' SUMMARY. [ARCH. PATH.]

ON THE USE OF HEAT, DESICCATION AND OXYGEN IN THE LOCAL TREATMENT OF ADVANCED PERIPHERAL VASCULAR DISEASE. ISAAC STARR JR., Am. J. M. Sc. **187**:498 (April) 1934.

Eleven patients with gangrene due to advanced peripheral vascular disease were treated by controlled heat, both moist and dry. For the relief of pain the optimum range of temperature was from 33 to 35 C.

Local applications of oxygen were made to the feet of seven patients having gangrene or other lesions. Concentrations of oxygen of 50 per cent or lower produced no change in color or sensation, but with concentrations above 80 per cent pain was relieved and the color improved.

When moisture was prevented from accumulating in the gas-tight oxygen cover, it was noted that wet gangrene was prevented from developing and that there was a tendency to convert a wet into a dry gangrene with lessened infection.

JAMIESON, Detroit.

THE TREATMENT OF PELLAGRA WITH CERTAIN PREPARATIONS OF LIVER. J. M. RUFFIN and D. T. SMITH, Am. J. M. Sc. **187**:512 (April) 1934.

In carrying out this work a standard basic diet was prepared which was lacking only in vitamin G (B_2). This diet consisted of 2,900 calories of fat meat, field peas, rice, hominy, cane syrup, brown gravy and lard, supplemented with 90 cc. of cod liver oil, 45 cc. of tomato juice, 6 Gm. of calcium gluconate, 6 Gm. of iron and ammonium citrate and 60 Gm. of cheese.

Three patients receiving this diet had a disappearance of the skin lesions, but the lesions returned on exposure to sunlight.

Ten patients who did not improve on the standard basic diet then received daily 90 cc. of aqueous extract of liver by mouth. Striking improvement began between the third and the fifth day and continued until recovery.

Five patients showed practically no clinical improvement with 5 cc. of liver extract given intramuscularly daily, but recovery was prompt when the aqueous extract of liver was given orally.

Exposure to sunlight in spring and summer was found to cause dermatitis in persons with active and potentially active pellagra but not in normal controls or in persons with pellagra who had received adequate treatment.

JAMIESON, Detroit.

OBSERVATIONS UPON SYPHILIS OF THE HEART, CORONARY OSTIA AND CORONARY ARTERIES: I. WITH SPECIAL REFERENCE TO THE CLINICAL PICTURE PRESENTED BY SYPHILITIC STENOSIS OF THE CORONARY OSTIA. M. C. PINCOFFS and WILLIAM S. LOVE JR., Am. J. Syph. & Neurol. **18**:145 (April) 1934.

Stenosis of the coronary ostia is of frequent occurrence in syphilitic cardiovascular disease and is the one lesion of the coronary arteries acknowledged by all to be of syphilitic origin. In this report the authors attempt to obtain, from the analysis of the cases and from their postmortem study, a clinical picture which will enable the physician to recognize occlusion of the coronary ostia in the living patient.

They conclude that from the time of the onset of symptoms the clinical course of occlusion of the ostia of the coronary arteries has been shown to be unusually brief and is characterized by a lack of response to therapy, a high incidence of the occurrence of anginal pain and a marked tendency to terminate with sudden death. One might define the coincidence of these factors in a given case as the "syndrome of syphilitic ostial stenosis."

REUTER, Milwaukee.

OBSERVATIONS UPON SYPHILIS OF THE HEART, CORONARY OSTIA AND CORONARY ARTERIES: II. WITH SPECIAL REFERENCE TO THE MYOCARDIAL LESIONS NOTED IN STENOSIS OF THE CORONARY OSTIA. W. S. LOVE JR. and C. GARDNER WARNER, Am. J. Syph. & Neurol. **18**:154 (April) 1934.

Data derived from the study of syphilitic heart disease lead the authors to conclude that the myocardial lesions noted in some cases can most readily be explained on the basis of a defective coronary circulation, and less frequently by some other associated morbid process. Obliterative endarteritis of the arterioles of the coronary arteries was the most commonly noted lesion. Stenosis of the coronary ostia produces the most marked myocardial lesions. No evidence of widespread syphilitic myocarditis and no Spirochaeta pallida or gummas were found in the cases studied. The thesbian vessels do not provide a very effective compensation for the loss of a large part of the coronary arterial system.

REUTER, Milwaukee.

THE GASTRIC DISTURBANCES SECONDARY TO SYPHILITIC INFECTIONS. J. FRIEDENWALD and S. MORRISON, Am. J. Syph. & Neurol. **18**:163 (April) 1934.

Syphilis plays an important rôle in the production of gastric symptoms. These symptoms may occur as the result of syphilitic lesions of the stomach itself or may be produced secondarily owing to a generalized systemic infection or to syphilitic involvement of one or many organs. The authors' report concerns particularly the disturbance of gastric function secondary to the presence of syphilis in the body. In such a consideration, the stomach may be secondarily involved as a result of a general syphilitic infection or as a result of syphilitic disease of special organs.

Gastric disturbances are noted both in early and in late syphilis, but by far the most common and important forms are observed as a result of the tertiary type. Involvement of the liver or of the nervous system is responsible for many of the gastric manifestations. The symptoms most commonly observed are nausea, vomiting, pain, eructation, distention and a feeling of fulness. These may vary greatly according to the location and extent of the syphilitic lesion. Neurosyphilis plays a most important rôle in the production of gastric symptoms, of which those

occurring as a result of tabes are of extreme interest. Gastric disturbances which cannot be accounted for must often be regarded from the standpoint of a possible syphilitic origin, and in many instances a syphilitic infection may be established as the probable cause. Disappearance of symptoms as the result of antisyphilitic treatment is confirmatory evidence of the correctness of the diagnosis.

REUTER, Milwaukee.

CHANCRE OF THE CERVIX. M. T. MORRISON, Am. J. Syph. & Neurol. **18**:196 (April) 1934.

Primary chancre of the cervix of the uterus is likely to show an incidence of from 14 to 18 per cent of all infectious syphilitic lesions in the female. In the author's experience three fourths or twelve of sixteen cases of chancre of the cervix have shown gross physical findings that were characteristic. These syphilitic ulcers are very moist, resembling somewhat a mild heat burn, with the area of the ulcer a pearly pink and not elevated above the adjacent cervical mucosa. The ulcers occur adjacent to the external os on one or both of the lips of the cervix and sometimes completely encircle the external os. In most of the author's cases there was observed at the introitus moderate to profuse discharge of a serosanguineous, nonpurulent character. Two of the author's sixteen cases were of the indurated, raised hunterian ulcer type, and two were of the swollen edematous type which filled the speculum. The cardinal complaints in their order of frequency were malaise with headache, an unnatural but menstrual-like discharge and hoarseness.

Dark-field examination is the most useful diagnostic procedure.

REUTER, Milwaukee.

GENERAL PARALYSIS. E. T. HOVERSON, Am. J. Syph. & Neurol. **18**:221 (April) 1934.

The author reports on twenty-five cases of dementia paralytica in which the patients were treated by injections of a preparation of cerebral lipoids in conjunction with the administration of tryparsamide. Remission occurred in 48 per cent in the twenty-five cases. The treatment was ambulatory, and there were no ill effects. This method offers a form of therapy which is applicable to all stages of neurosyphilis. The beneficial effects noted may be induced by stimulation of the oxidation-reduction mechanism, or its regulation, or they may be based on the formation of antibodies. This phase of the subject is being investigated.

REUTER, Milwaukee.

NEVUS PILOSUS PIGMENTOSA CONGENITA: ITS SKIN RESPONSES TO DRUGS. MORTON S. STERN, New England J. Med. **209**:694 (Oct. 5) 1933.

This study was undertaken to obtain information as to whether an abnormally pigmented and hairy area caused by increased ectodermal tissue differed basically in physiologic activity from the normal tissue. A case of pigmented and hairy nevus of the "bathing drawer" variety is presented in detail. The cutaneous reactions of the nevi and normal skin were compared and the following observations made: 1. The response of the abnormal skin to epinephrine was more rapid, more extensive and of longer duration than that of normal skin. 2. The response of the nevus to atropine was more retarded, more extensive and of longer duration. 3. Histamine evoked a delayed reaction, a greater response and one of longer duration in the pigmented area. 4. The reaction to pilocarpine was delayed and of longer duration in the nevus than in the normal tissue. 5. Physostigmine showed practically no reaction in the nevus.

GENGENBACH, Denver. [AM. J. DIS. CHILD.]

SEVERE GOLD INTOXICATION DESPITE SMALL DOSES: CUTANEOUS MANIFESTATIONS AND BLOOD CHANGES. M. ARMAND-DELILLE, GAVOIS and V. BAYLE, Bull. Soc. de pédiat. de Paris **30**:654 (Dec. 20) 1932.

A girl, 14 years old, who had pulmonary tuberculosis, was given injections of small doses of a preparation containing gold. Signs of intoxication developed, chief of which were a digestive disturbance, a reddened throat, an urticarial cutaneous rash with some purpuric lesions, metrorrhagia and leukopenia with agranulocytosis. The patient was subject to an urticarial eruption of the skin after eating egg and fish, and it is thought that she had some sensitivity to gold salts. She received six injections of gold sodium thiosulphate totaling 0.7 cg. over a period of six weeks. Signs of intoxication appeared two months after the first injection.

BENJAMIN, Montreal, Canada. [AM. J. DIS. CHILD.]

CONGENITAL SYPHILIS IN A CHILD SHOWING REPEATED SIGNS OF ACTIVITY WHICH SUBSIDED RAPIDLY BUT NOT PERMANENTLY WITH SPECIFIC TREATMENT. M. LINOSSIER-ARDOIN, Bull. Soc. de pédiat. de Paris **30**:674 (Dec. 20) 1932.

A girl, 8½ years old, had mucocutaneous lesions at the age of 20 days, an ocular lesion at 2 years and multiple lesions of the bones at 4 years; all of these subsided promptly under antisyphilitic treatment and remained quiescent for varying periods. The child showed some involvement of one eye, and the Wassermann reaction was strongly positive. It is emphasized that the treatment was inadequate. Although the clinical signs cleared up each time when some antisyphilitic therapy was administered, the cure was only apparent and fleeting. Before the child is considered cured treatment should be persisted in for at least two years, and the Wassermann reaction should become negative and remain negative when repeatedly checked at frequent intervals. At the return of even the slightest positive reaction treatment should be resorted to at once and continued until the reaction turns negative and remains so when repeatedly checked. The clearing up of the clinical manifestations of syphilis is not to be used as a guide for the amount of treatment necessary.

BENJAMIN, Montreal, Canada. [AM. J. DIS. CHILD.]

CONGENITAL SYPHILIS. JEAN OLIVER, Progrès méd., July 29, 1933, p. 1354.

The fetus may be contaminated from the mother in any month of pregnancy. The usual way is from the placenta; certainly contaminations during birth are exceptional. The effect of treatment of the mother on the fetus is so variable that one cannot say with certainty that the child will show protection when born. Likewise, as to the time during pregnancy when the mother is infected, the effect on the child is variable. The entire subject may be summed up in saying that a syphilitic woman should be very carefully treated and examined before being allowed to marry, as she is likely to carry the disease in a latent stage. If it is not certain that the woman is free from syphilis, she should be actively treated during pregnancy. If there is any question of a mother having syphilis in a latent stage, and the prenatal treatment was inadequate, the infant should be treated regardless of an apparently normal physical condition.

SANFORD, Chicago. [AM. J. DIS. CHILD.]

CONGENITAL SYPHILIS OF THE BONES IN EARLY INFANCY. M. PEHU and A. POLICARD, Paidoterapia **12**:425 (Sept.) 1933.

The spirochete invades the skeleton of the fetus very quickly and attacks the bones of cartilaginous origin. The osseous lesions are symmetrical. The authors propose a division into five classes: (1) osteochondritis, (2) periostitis, (3) osseous rarefactions, (4) hypertrophy of the bones and (5) transverse bands on the metaphyses. Osteochondritis appears first in intra-uterine life and is the forerunner of periostitis. The bony rarefactions and hypertrophies are easily seen by

x-ray picture. The transverse bands are present on the diaphysis just back of the epiphysis and are more easily seen in the long bones. The x-ray picture is of great value as an aid to diagnosis.

HERRON, Spokane, Wash. [AM. J. DIS. CHILD.]

A CASE OF DYSHYDROTIC, SUPERFICIAL CUTANEOUS ACTINOMYCOSIS OF THE PALMS AND SOLES. PING TING HUANG, Dermat. Wchnschr. **97**:1679 (Dec. 2) 1933.

A pompholyx type of eruption occurred on the palms and soles of a 32 year old woman. An aerobic actinomycete was recovered in the cultures. It closely resembled Actinomyces bovis (Harz, 1877) and Actinomyces keratolyticus (Acton and McGuire, 1931) but produced neither red nor black pigment.

TAUSSIG, San Francisco.

PSORIASIS AS AN ALLERGIC CONDITION. M. MEINICKI and C. RYLL-NARDZEWSKI, Dermat. Wchnschr. **97**:1685 (Dec. 2) 1933.

The authors argue for the allergic nature of psoriasis. They have found that in about one third of their patients with psoriasis intracutaneous injections of dmelcos or staphylococcus vaccine caused a focal reaction in the lesions. They point out that various types of irritation to the skin of a patient with psoriasis may cause the development of psoriatic lesions. TAUSSIG, San Francisco.

MYXEDEMA CIRCUMSCRIPTUM TUBEROSUM PLANUM SYMMETRICUM CRURUM IN EXOPHTHALMIC GOITER. J. J. ZOON, Dermat. Wchnschr. **97**:1694 (Dec. 2) 1933.

The patient, a 47 year old woman, had a typical exophthalmic goiter. She had been operated on twice, but her symptoms recurred. On both legs were oval circumscribed elevations the size of a man's palm. In the histologic sections mucin was demonstrated in the reticular layer. TAUSSIG, San Francisco.

LUPUS SARCOMA. A. SCHOCH, Dermat. Wchnschr. **97**:1723 (Dec. 9) 1933.

The author briefly describes two instances in which mixed cell sarcomas developed in the lesions of lupus vulgaris. TAUSSIG, San Francisco.

SCLERODACTYLIA. L. S. SIROTA, Dermat. Wchnschr. **97**:1731 (Dec. 9) 1933.

The author describes in detail the findings in a case of sclerodactylia. Various forms of therapy, including periarterial sympathectomy, proved to be of no value.

TAUSSIG, San Francisco.

TYLOSITAS SYMMETRICA POLLICIS ET INDICIS. HUGO STANKA, Dermat. Wchnschr. **97**:1730 (Dec. 9) 1933.

Symmetrical keratoses developed on the tips of the thumbs and index fingers of an insane patient. They were apparently the result of repeated cigaret burns.

TAUSSIG, San Francisco.

LICHEN RUBER PLANUS AS AN ISOMORPHIC EFFECT OF IRRITATION FROM GOLD THERAPY. R. LEWITH, Dermat. Wchnschr. **97**:1751 (Dec. 16) 1933.

Following a course of injections of a gold salt for arthritis deformans, a dermatitis developed. This developed into an eruption resembling lichen ruber planus. The histologic picture was that of lichen planus. The author concludes that this phenomenon is to be considered as a nonspecific irritative effect.

TAUSSIG, San Francisco.

TREATMENT OF LYMPHOGRANULOMA INGUINALE. FRIEDRICH KALZ and FELIX SAGHER, Dermat. Wchnschr. **97**:1754 (Dec. 16) 1933.

Thirty cases of lymphogranuloma inguinale were treated with convalescent serum. The course of the disease was shortened to an average of six weeks.

TAUSSIG, San Francisco.

CLINICAL INVESTIGATION AND PATHOLOGIC HISTOLOGY OF THE ENDOCRINE GLANDS IN SCLERODERMA. JENÖ FOLLMANN and BÉLA BALLÓ, Dermat. Wchnschr. **97**:1779 (Dec. 23) 1933.

Two patients with scleroderma were studied intensively. One came to autopsy, and on microscopic examination changes were noted in the endocrine glands. This strengthens the conclusion that the disease is an unbalance of the endocrine secretions in close association with the disturbance of the sympathetic nervous system. It should be treated by specific glandular products as well as by the usual symptomatic methods.

TAUSSIG, San Francisco.

QUANTITATIVE CLOUDING REACTIONS (TRÜBUNGSREAKTIONEN) AS A MEASUREMENT OF THE PROGRESS OF THERAPY IN SYPHILIS. C. STERN, Dermat. Wchnschr. **97**:1788 (Dec. 23) 1933.

The author describes the use of a quantitative citochol reaction and indicates in a series of tables its value in judging the effectiveness of a course of antisyphilitic therapy.

TAUSSIG, San Francisco.

LIVER THERAPY OF PSORIASIS. THEODOR GRÜNEBERG, Dermat. Wchnschr. **97**:1793 (Dec. 23) 1933.

During the past two years liver extract has been given intramuscularly to patients with psoriasis in addition to other forms of therapy. It apparently has improved the results and decreased the tendency to recurrence. The mechanism is not clear but may be connected with the influence on the sulphur content of the skin.

TAUSSIG, San Francisco.

THE NATURE OF PITYRIASIS ROSEA. P. PHOTINOS, Dermat. Ztschr. **68**:187 (Jan.) 1934.

The author concludes that the true nature of pityriasis rosea is still unknown. Clinical as well as microscopic observations speak for an ectogenous genesis. The "spores" of Du Bois were demonstrated in each of four cases studied. One of the cases developed following the wearing of new, unlaundered underclothing. Two of the cases occurred in women who were living together.

TAUSSIG, San Francisco.

PITYRIASIS RUBRA PILARIS. WILHELM SCHILLING, Dermat. Ztschr. **68**:190 (Jan.) 1934.

Seven cases of pityriasis rubra pilaris were studied. The various theories as to the etiology are discussed, and the author concludes that it is possible that various etiologic factors may produce the same clinical picture.

TAUSSIG, San Francisco.

A RARE MANIFESTATION OF SENSITIVITY TO NEOARSPHENAMINE. L. S. SIROTA, Dermat. Ztschr. **68**:198 (Jan.) 1934.

About one minute following the second injection of neoarsphenamine the patient complained of severe pain in the buttocks and sacral regions and stiffness of the

back, associated with flushing of the face and dilatation of the pupils. The reaction lasted about three minutes. The third injection of a smaller dose was given slowly, but the reaction was the same. An injection of 1 cc. of 1:100 epinephrine previous to the following injections prevented the reaction.

TAUSSIG, San Francisco.

EPIDERMOPHYTIDS AND EPIDERMOPHYTIN. A. E. RUETE and URSULA SCHOLZ, Dermat. Ztschr. **68**:241 (Feb.) 1934.

The development of epidermophytids and the positive outcome of the intradermal epidermophytin test are cited by Ruete and Scholz as proof that epidermophytosis is not merely a superficial disturbance. They found that vaccination with epidermophytin (filtrate from epidermophyton cultures) gave positive results in 100 per cent of the patients with epidermophytosis. Moreover, the reaction seems to be specific for epidermophytosis, for it was negative in a form of trichophyton infection and in pityriasis versicolor. However, further tests will be necessary to demonstrate the specificity definitely. The experiences with the immunoreaction induced the authors to try the therapeutic application of epidermophytin. They treated fifteen patients by the production of epidermophytin wheals and effected prompt cures. The injections are not painful. With the exception of a slight itching, they produce no undesirable sensations and no fever. The authors cite case reports which indicate that the injections hasten the frequently prolonged course of the disorder and that in combination with iodine and a sulphonated bitumen powder they may replace the unpleasant treatment with ointments.

[J. A. M. A.]

A CASE OF VERRUCA PERUANA (CARRION'S DISEASE). W. FROHN, Dermat. Ztschr. **68**:245 (Feb.) 1934.

A case of verruca peruana was observed at Innsbruck. The patient, a 29 year old man, had been ill while on an expedition in the Andes in South America. The sickness followed the bite of an insect. He lost considerable weight, and on his return to Europe numerous angiomatous tumors developed, scattered over the face, neck, trunk and extremities. Bartonella bacilliformis was not demonstrated in the blood smears. Histologic examination verified the diagnosis of verruca peruana. Various types of local therapy proved unavailing, including radiotherapy. Arsphenamine, six injections with a total dose of 3.45 Gm., resulted in a complete cure, including a return to normal weight.

TAUSSIG, San Francisco.

EXPERIMENTAL HERPETIC FOLLICULITIS: PERCUTANEOUS INOCULATION WITH HERPES AND THE PROBLEM OF NATURAL TISSUE INFECTION. H. HRUSZEK, Dermat. Ztschr. **68**:258 (Feb.) 1934.

Hruszek shows that the manifestations which have been traced to the herpes virus are manifold. As the port of entry of the herpes virus and the mechanism of its first infection have not been fully explained, the author made studies with percutaneous inoculation. Inoculation of human skin was accomplished by rubbing it with human herpes material. A typical herpetic folliculitis developed. The herpetic nature of the folliculitis was demonstrated on the cornea of rabbits and in further human passages by means of scarification. The further development of the herpes that was produced by rubbing herpes material into the skin and its tendency to successive crops and to relapses were identical with those of the herpes that had been produced by scarification. The author thinks that there are perhaps other forms of simple herpes, in which a herpetic etiology has not been thought of. He mentions particularly follicular dermatoses (according to Naegeli some cases of "nonparasitic" sycosis) that do not necessarily have to present a vesicular monomorphic picture but may appear also as papules, urticarial efflorescences and pustules.

[J. A. M. A.]

OSTEITIS TUBERCULOSA MULTIPLEX CYSTICA, WITH SARCOID AND INVOLVEMENT OF THE HILAR NODES. WILHELM BAYER, Jahrb. f. Kinderh. **138**:31 (Jan.) 1933.

A case was observed for a period of four years. At no time did the results of tuberculin tests or animal inoculations point to tuberculosis.

CLAUSEN, Rochester, N. Y. [AM. J. DIS. CHILD.]

FURRED TONGUE IN GENERAL DISEASES. F. KLEE, Monatschr. f. Ohrenh. **68**:129 (Feb.) 1934.

Klee examined the tongues of 434 patients whose underlying disease state had been carefully studied. Furring of the tongue was found in 310 (71 per cent). It occurred in general diseases as well as in those of the oral cavity and could not be considered a specific manifestation in any instance. It occurred in varying degrees in all smokers and tobacco chewers. The author concludes that furring of the tongue allows no conclusion to the nature of a disease.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

CLINICAL AND EPIDEMIOLOGIC SIGNIFICANCE OF ERYTHEMA NODOSUM IN CHILDREN. J. BROCK, München. med. Wchnschr. **80**:1087 (July 14) 1933.

From data collected mainly in Scandinavian countries it has been found that in practically all children in whom erythema nodosum occurs it is a manifestation of tuberculous infection. It frequently develops at the end of the biologic period of incubation, at the time when the skin first becomes sensitive to tuberculin. During the course of erythema nodosum the skin is highly sensitive to tuberculin, reacting to it in high dilutions. There is an increase in the rate of blood sedimentation. In many cases repeated roentgenologic examinations will show active lesions involving the pleura, parenchyma of the lungs or hilar nodes. Every case of erythema nodosum in childhood means a new tuberculous infection and indicates the presence of a carrier in the child's environment. This is of great epidemiologic significance. The treatment of erythema nodosum is that of tuberculosis.

BRAHDY, Mount Vernon, N. Y. [AM. J. DIS. CHILD.]

CIRCUMSCRIBED FACIAL HYPERHIDROSIS. A. I. GESCHELIN, Ztschr. f. Hals-, Nasen- u. Ohrenh. **35**:168 (Feb. 10) 1934.

Geschelin describes the case of a patient, aged 22, who had suffered from increased perspiration of the face, especially the left side, for nine years. This was especially marked during eating. Chewing a piece of herring, for example, caused great drops of sweat to appear on the face, neck and upper part of the thorax. Drinking water caused only slight hyperemia of the face. The patient had typhus in 1920, which was complicated by inflammation of the left parotid gland for which surgical intervention was necessary. The author agrees with Vogel as to the essential sympathetic-parasympathetic mechanism but thinks that much detail remains to be clarified.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THERAPEUTIC EXPERIENCE WITH PILOCARPINE IN LUPUS PERNIO. NAOHIDE OGAWA, Jap. J. Dermat. & Urol. **35**:313 (March) 1934.

In the two patients shown the feet were the parts involved, and in each the condition had become progressively worse despite a variety of treatments until finally large ulcers were present in addition to the usual discoloration, swelling and painfulness of chilblains. The injections of pilocarpine in the tests of the vegetative nervous system did not produce any sweating in the affected skin areas, and this led the author to try the direct application of pilocarpine in the form of a 1 per cent salve, on the theory that the vasomotor and trophic disturbances

are the result of injury to the vegetative nerves supplying these areas. After a few days of this treatment the ulcers in both cases exhibited healthy granulations, and within two or three weeks they had healed over completely and the affected areas as a whole had assumed a normally pink, warm and tumid appearance with the rapid subsidence of all painful symptoms. BRENNAN, Chicago.

A CASE OF PITYRIASIS CIRCINATA TOYAMA. TAKAHIRO MORIKAWA, Jap. J. Dermat. & Urol. **35**:318 (March) 1934.

The author demonstrates an example of Toyama's pityriasis in a 19 year old girl without a familial or personal history of tuberculosis. Four months prior to this report erythematous flecks suddenly appeared on the back. There were no subjective symptoms when they appeared, but they later spread and the patient stated that there was mild itching at times. At the time of writing the spots were located chiefly on the back and in one place on the loin. They were flat, round to oval, light brown and about the size of a quarter. In places they had become confluent, and when scratched they desquamated in fine scales. The scales histologically and culturally revealed no causative organism. Histologic examination revealed hyperkeratosis (pronounced in places), acanthosis, absence of inflammatory infiltrations and hyperpigmentation. BRENNAN, Chicago.

METASTATIC KERATITIS PARENCHYMATOSA IN SYPHILITIC RABBITS: I. DISTRIBUTION OF SPIROCHAETA PALLIDA IN THE EARLY STAGE. T. FUNABASHI, Lues: Bull. Soc. japon. de syph. **10**:131 (Feb.) 1934.

Sixty-nine rabbits were inoculated in a testicle or under the scrotum with an emulsion or pieces of syphilitic testicles. From the time of appearance of orchitis the eyes were carefully examined, and the cornea was trepaned and examined for spirochetes. The following observations were made: Pericorneal injection of blood vessels and edema which developed a certain time after the appearance of the chancre were in most cases the forerunners of parenchymatous keratitis. Of forty-five eyes with pericorneal injection and edema, spirochetes were found in seven within from forty to seventy days after infection. In one eye spirochetes were seen nineteen days after infection. Of sixteen eyes in which the corneal opacity was particularly marked, spirochetes were found in eight within from fifty to eighty days after infection. In eyes showing localized opacity, spirochetes were seen only in that spot; in those with diffuse opacity they were disseminated all over the cornea. Of three eyes which showed marked new formation of capillaries, spirochetes were found in two within from sixty to seventy days in the progressing border of the newly formed capillaries as well as in other places. Increase of spirochetes is parallel with the development of the cardinal symptoms of parenchymatous keratitis, namely, the opacity and new formation of capillaries. In fifty-four such eyes spirochetes were found from fifty to ninety days after infection.

BLOOM, New York.

SPIROCHETES IN THE LYMPH GLANDS OF SYPHILITIC RABBITS: II. FLUCTUATION IN THE SPIROCHETE CONTENT OF THE SPLEEN. S. WATANABE, Lues: Bull. Soc. japon. de syph. **10**:147 (Feb.) 1934.

Rabbits in different stages of infection following testicular inoculation with syphilitic material were investigated for the content of spirochetes in the spleen. The spleen was emulsified and injected in different dilutions into the backs of healthy rabbits. It was found that the spleen harbors spirochetes on the sixth day of the infection, the number increasing until the end of one month. Spirochetes are still present after fifty days, but they are considerably fewer or absent after one hundred days. Inoculation with an emulsion of spleen removed two hundred days after infection always gave negative results. By this method it was found

that the number of spirochetes in the spleen is subject to great fluctuations in the course of the infection. This finding coincides with the observation made in the experiment with lymph glands.

BLOOM, New York.

PASSIVE IMMUNITY TO SYPHILIS IN RATS. K. YASUMOTO, Lues: Bull. Soc. japon. de syph. **10**:178 (Feb.) 1934.

Blood serum of rabbits which had been infected from three to eight months previously with syphilis was inactivated, and 0.5 cc. was injected into the scrotum of rats every second day, from seven to eleven injections being given. Simultaneously with or following this procedure the same amount of an emulsion of syphilitic virus was injected into the same location. The iliac lymph nodes of the rats were then examined for spirochetes. Contrary to expectation it was found that the lymph nodes of rats which received repeated injections of syphilitic serum contained more spirochetes than the control animals which received normal serum.

BLOOM, New York.

EXPERIMENTAL YAWS IN MICE: I. SPIROCHAETA PALLIDA IN THE ILIAC LYMPH GLANDS. H. MISAIZU, Lues: Bull. Soc. japon. de syph. **10**:162 (Feb.) 1934.

Mice infected with Spirochaeta pallida showed no clinical symptoms except swelling of the iliac lymph glands, which gradually softened and decreased in size. In the swollen glands mobile spirochetes were found on microscopic examination. After a certain time the spirochetes diminished in number, and they finally disappeared. After scrotal infection spirochetes could be demonstrated in the glands from twenty to fifty days following the inoculation; after peritoneal inoculation it took from thirty-five to fifty days.

BLOOM, New York.

CLINICAL STUDY OF PERIOSTITIS AND OSTITIS IN THE EARLY STAGE OF FRAMBESIA. K. ISEKI, Lues: Bull. Soc. japon. de syph. **10**:186 (Feb.) 1934.

The author reports two cases of ostitis and periostitis developing in an early stage of yaws. In one case, that of a 19 year old girl, there was a spindle-shaped swelling of the second phalanx of both middle fingers which developed one year after the infection. The other case was that of a 10 year old girl who had a similar involvement of the first phalanx of one index finger and the middle portion of the left tibia. The bone lesions developed from two to three months following the infection.

In both cases the lesions healed rapidly under treatment with arsphenamine.

BLOOM, New York.

LEPROSY IN AUSTRIA. W. FROHN, Acta dermat.-venereol. **15**:1 (March) 1934.

The author discusses the different forms of leprosy and the incubation period and the historical aspects of the disease. He states that there are from 3,000,000 to 5,000,000 of people in the world who are suffering from this disease. For more than a thousand years leprosy spread and was feared in Austria as a pestilence. It reached its acme in the thirteenth century. The author explains this by the fact that at this time continuous warfare and danger caused the cities to surround themselves with permanent walls and canals, which forced the growing population to live under the most unhygienic conditions and thus increased the contagiousness of leprosy. The crusades also had some influence in the spreading of this disease. The traces of the leprous past are preserved in the art of Austria up to the present time. In the fight against leprosy the only weapon was isolation of the diseased. It was carried out energetically by the church, state, cities and medical profession. As soon as the diagnosis was definitely established the unfortunate persons were removed to special small hospitals which were situated outside the city gates in

the fashion of small leper colonies. Through very strict isolation and through the betterment of the social, hygienic and medical conditions this disease was practically exterminated in the eighteenth century.

ASTRACHAN, New York.

SILK HANDLERS' DISEASE OF THE SKIN. HERMAN GOODMAN, Acta dermat.-venereol. **15**:25 (March) 1934.

The author discusses the prevalence of a dermatitis among workers in a throwing mill, where raw silk was prepared for weaving. He gives a detailed account of two patients with "silk handlers' dermatitis" and mentions eight other cases which came under his personal observation. He also gives information on silkworm culture, silk cocoon unreeling and silk throwing and the composition of some of the solutions used in silk throwing. A case of silk allergy is described, and the literature on the subject is reviewed. As a result of patch tests and past experiences the author believes that the cause of dermatitis in susceptible persons in the silk mill was the component of an antimildew solution similar to crude cresol. He mentions a case of dermatitis due to compound solution of cresol and gives a detailed description of the origin and characteristics of the cresols. He discusses the problem of preventing silk handlers' disease of the skin and comes to the conclusion that the only way to do so is to substitute for the cresol component of the antimildew solution chemicals which are not irritating to masses of people.

ASTRACHAN, New York.

THE ANGIONEUROTIC SYMPTOM COMPLEX DURING TREATMENT WITH ARSPHENAMINE. H. C. GJESSING, Acta dermat. venereol. **15**:59 (March) 1934.

The author cites six cases in which a nitritoid reaction developed following treatment with arsphenamine and discusses the different clinical types of this reaction. The most important ones are (1) the red angioneurotic crisis and (2) the white angioneurotic crisis. The latter is very dangerous and is characterized by cadaver-like paleness or cyanosis of the face, edema of the face, absence of pulse and unconsciousness. There are also intermediate forms.

In none of these six cases did the reaction occur after the first injection; it usually appeared after a comparatively long course of injections was given. Several of the injections previous to the crisis were followed by signs of beginning intolerance (fever, indisposition). The author is of the opinion that the angioneurotic crisis is caused not by too large doses of the drug but by congenital or acquired predisposition of the patient. He believes that hepatic insufficiency may play an important part in the production of this reaction.

ASTRACHAN, New York.

LIPOID IMBIBITION OF THE DEGENERATE ELASTIC TISSUE. ERICH URBACH, Acta dermat.-venereol. **15**:69 (March) 1934.

The author divides all lipoidoses into two groups: (1) generalized lipoidoses, in which a primary disturbance of fat metabolism exists, and (2) local lipoidosis, in which a local tissue disorder is followed by secondary fat deposition. In cases of senile weather skin there is always noticeable clinically a yellowish hue, which may be explained by imbibition (passive deposition) of lipoids among the degenerated broken-up elastic tissue fibers. Microscopically, the damaged elastic tissue, on sudan III staining, takes a brownish-red color, due to imbibition of lipoid in it. The author rejects the theory of lipoid degeneration of tissues, because the direct formation (genesis) of fats from proteins could not be proved in animals or human beings.

ASTRACHAN, New York.

Society Transactions

NEW YORK DERMATOLOGICAL SOCIETY

R. H. Rulison, M.D., *Secretary*

Regular Meeting, Feb. 27, 1934

Edward R. Maloney, M.D., *President*

(*Concluded from p. 483*)

Chronic Pigmentation and Dermatitis of the Neck (Poikiloderma?). Presented by Dr. Fred Wise.

This woman, aged 41, born in the United States, first came to the skin clinic of the New York Post-Graduate Medical School and Hospital on Dec. 2, 1933. She presents indefinitely defined areas of hyperpigmentation on the sides and back of the neck extending onto the cheeks over the angles of the jaws. She states that the pigmentation started two years ago, that it has been associated with mild itching and that she had not employed any irritating cosmetics or other skin irritants prior to the appearance of the dermatitis.

On close examination, the lesions appear to consist of numerous finely dilated capillaries associated with faint pigmentation and superficial wrinkling of the skin of the neck. There are no evidences of atrophy, but the possibility of poikiloderma of Civatte and pseudo-atrophoderma colli is considered.

On exposure of the right shoulder to a suberythema dose of ultraviolet radiation from a quartz mercury vapor arc lamp, the patient reacted with mild erythema.

General medical examination and urinalysis gave negative results. The Wassermann reaction was negative.

DISCUSSION

Dr. F. C. Combes: This eruption presents many interesting characteristics, and I do not see how one can make a definite diagnosis by clinical observation. There is some evidence that suggests poikiloderma of Civatte. The condition does not strike me as being the same as pseudo-atrophoderma colli, a case of which was recently reported (Arch. Dermat. & Syph. **29**:53 [Jan.] 1934). First, its long duration is against that diagnosis. If I recall correctly, the patient in the case just cited got well spontaneously. Secondly, there seems to be no suggestion of atrophy but merely pigmentation and erythema. I think that the possibility of chloasma should be considered.

Dr. George M. MacKee: I agree with Dr. Combes that chloasma should at least be considered. The patient states that the eruption started on her cheek as a brown macule which eventually almost disappeared. It is slightly evident now. The condition then spread to the neck. It is unusual to have chloasma anywhere but on the face, but the fact that the lesions are on the neck does not necessarily exclude chloasma.

Dr. Eugene F. Traub: With the hasty examination necessary this evening, it is difficult to be certain, but I gained the impression that the patient presents an itching dermatosis that may be lichenoid. The pigmentation seems to be about what one would expect in this location. She has a short haircut which further exposes her neck to wind, weather and sunlight. The pigmentation definitely impresses me as being normal for such an exposed location.

A Case for Diagnosis (Pemphigus?). Presented by Dr. Eugene F. Traub.

This man, aged 34, a clerk, states that the present condition was first noted on the face about fifteen years ago. Small blisters which dried and were soon

covered with large crusts continued to appear. The condition remained localized for a long time and then spread from the right side of the nose; it now involves the greater portion of the face, scalp and neck. The lesions came and went, a blister running its course in from about ten days to two weeks. The patient says that he has not taken any medicine. He states that although he has almost constantly been under the care of some physician, no treatment has caused any material improvement except on one occasion when he had a remission of a little over a year. As the patient was seen for the first time yesterday, there are no laboratory data.

DISCUSSION

DR. FRED WISE: I think that the eruption is either a staphylococcic or a streptococcic follicular infection which is resistant to treatment. I do not think that it is pemphigus or lupus erythematosus.

DR. R. H. RULISON: I agree with Dr. Wise. I think that the condition is an impetiginous eruption of an unusual type. It is probably recurrent because it becomes quiescent in the follicles and then flares up again.

DR. GEORGE M. MACKEE: I did not see any folliculitis. The elementary lesion is a vesicle which later ruptures and becomes crusted. Dermatitis artefacta and localized pemphigus are possibilities. I understand that bromoderma and iododerma have been excluded.

DR. HOWARD FOX: If the condition is folliculitis, why does it avoid the hairy region?

DR. EUGENE F. TRAUB: I hoped that we should be able to send a report to Washington, D. C., on the diagnosis. The man has been treated by a number of dermatologists there over a period of many years with all kinds of local remedies, including different types of lamps, roentgen rays, etc., with little or no influence on the eruption. However, he has remissions from time to time, either with or without treatment, when the condition almost disappears. Many of the lesions are in areas where folliculitis might be expected, but this does not seem to be a likely possibility in view of the course of the disease. I agree with Dr. MacKee that it may be pemphigus of unusually slow development.

PARAPSORIASIS GUTTATA. Presented by DR. FRED WISE.

E. E., a man aged 25, appeared for treatment at the skin clinic of the New York Post-Graduate Medical School and Hospital on Feb. 10, 1934. He presents a widespread eruption, affecting chiefly the torso, of three months' duration. He complains of moderate itching. The eruption consists of several hundred small, flat, yellowish and somewhat violaceous papules, together with yellowish macules, chiefly on the back and chest. The lesions are in various stages of evolution, thus resembling so-called pityriasis lichenoides et varioliformis acuta, but there are no lesions with depressed centers. The Wassermann test was negative. Histologic examination showed a moderately mild exudative inflammatory process which might well fit in with the clinical diagnosis of parapsoriasis guttata, but the edema of the epidermis usually present in that condition was marked in the section.

DISCUSSION

DR. HOWARD FOX: I agree with the diagnosis.

DR. H. H. WHITEHOUSE: I should favor the diagnosis of pityriasis rosea even if I had no knowledge of a sentinel patch.

DR. F. C. COMBES: I think that in this case one is entirely at the mercy of the histopathologists.

EXTENSIVE PEMPHIGOID ERUPTION IN AN INFANT. Presented by DR. HOWARD FOX.

Baby K., a boy aged 9 months, has suffered from an eruption for two months. It appeared first on the face, after which it spread to the neck, chest and trunk,

especially the genital region, inner aspect of the thighs and lower part of the abdomen. At the age of 3 months the patient was vaccinated for smallpox, but this did not "take." The only medicine that he had received previous to the onset of the eruption was 4 drops of a proprietary preparation of barbituric acid. This was administered a month before the beginning of the eruption. None of those who had come in contact with the child had impetigo, including his parents and a sister, aged 6 years. The patient had been in excellent health. The Wassermann and Kahn tests were negative, and cultures of material from unbroken, clear bullae were sterile. Blood cultures were also sterile.

The eruption is symmetrical and consists of vesicles and small bullae arising for the most part on normal skin. They rupture easily and leave reddish abraded areas with shreds of epidermis at the periphery. Many have coalesced to form diffuse patches which are tender and apparently cause great discomfort. Some of the lesions, especially on the face, show evidences of secondary infection which may account for frequent moderate elevations of temperature. The patient demonstrates the presence of itching by efforts to rub his back and legs on the bed, but there are no scratch marks. There are no lesions in the mouth. The general condition is good, the baby being well nourished and vigorous. He is bottle fed and has gained 8 ounces (226.8 Gm.) since his illness.

DISCUSSION

Dr. George M. MacKee: It is difficult to rule out pemphigus, but Dr. Fox seems to have done so. The condition does not look like erythema multiforme because the bullae occur on the unaltered skin. The Nikolsky sign is absent, there are no lesions in the mouth and the patient is in good health. In spite of this the eruption clinically looks like pemphigus. Drugs have been ruled out, I understand. Therefore, I do not know what to call the condition except pemphigus vulgaris in an infant. Those who insist that there is no such thing as benign pemphigus will prefer to call it pemphigoid. It might be well to have a phytopharmacologic test made. It is my impression that vaccinia and pemphigoid eruptions following vaccination occur within a week or two subsequent to vaccination, which was not the case here.

Dr. J. Frank Fraser: I should like to add a word in regard to the diagnosis of true pemphigus and pemphigus neonatorum. As I understand it, pemphigus neonatorum is a streptococcic disease. In this case the contents of the unaltered bullae were negative for streptococci. That fact alone in my opinion supports strongly the view of Dr. MacKee that the condition is pemphigus vulgaris.

Dr. Eugene F. Traub: I do not believe that any one can give this eruption a specific name today with any degree of certainty. All of the members apparently have the same idea as to its classification. It recalls to my mind a number of cases I have seen in the past. One was a case of Dr. Williams' in which the eruption was similar to this one and which he labeled postvaccinal pemphigus, the eruption occurring in a young boy some time following a vaccination; after prolonged course, it eventually cleared up. Another case with lesions the counterpart of these occurred in a girl 17 years of age; she was presented before this society at successive meetings, at the first of which every one thought the condition was erythema multiforme with bullous lesions. At the following meeting, all agreed that it was pemphigus. The eruption cleared up with small doses of neoarsphenamine and has not recurred. Therefore, I believe there are many cases of this character which have a favorable prognosis as compared to the cases of true pemphigus.

Dr. F. C. Combes. I look at this case much as Dr. Traub does in relation to the vaccination. The introduction of a foreign protein such as vaccine may cause all sorts of eruptions, frequently of a bullous nature. There are many cases in the literature of bullous eruptions occurring at varying intervals after vaccination. I have no suggestion as to treatment because I have not treated any patients with such a condition.

DR. H. H. WHITEHOUSE: This is certainly an interesting case. I think that Dr. MacKee has differentiated the various lesions, and the condition undoubtedly looks like pemphigus. Postvaccinal eruptions do simulate pemphigus and erythema multiforme. The sterile contents of the bullae seem to point to the fact that the eruption is not pemphigus neonatorum or impetigo contagiosa. I agree entirely that the patients recover. This is one of the forms of true pemphigus pruriginosus in which the patients get well. I believe that it is due to a foreign protein. I do not know how to treat it.

DR. J. J. ELLER: I think that Dr. Traub's suggestion is good, and I feel as he does. I think that the condition is a postvaccinal eruption resembling pemphigus vulgaris.

DR. FRED WISE: I regard the eruption as pemphigoid but not pemphigus, as the general health of the patient seems unaffected and there are no lesions of the buccal and genital mucosae. I think that the child will fully recover.

DR. HANS J. SCHWARTZ: I do not see exactly how one can exclude bullous impetigo contagiosa. I had the opportunity of following many patients with such eruption in the old Lying-in Hospital, and this patient's lesions are characteristic in their distribution around the nose, mouth, neck, axillae and groins. Repeated cultures from the vesicles in my cases were negative except for the presence of Staphylococcus aureus. The material, however, was not necessarily taken from unbroken vesicles, and I do not know whether one can attach much importance to the presence of staphylococci. The eruptions varied from ordinary impetigo contagiosa to the severe type spreading all over the body and resulting in death in four or five days. At autopsy in two or three cases, nothing significant was found. Blood cultures were negative. As far as treatment is concerned, many remedies were tried including ammoniated mercury, sulphonated bitumen, etc. The treatment that seemed to give the best results was keeping the skin dusted with an ordinary dry dusting powder and maintaining the body heat.

DR. P. S. STAHL (by invitation): I should like to answer several questions which have been asked. The vaccination for smallpox was made four months before the appearance of the eruption, but it did not "take." There has been no impetigo or chickenpox in the family. The patient's sister, aged 6 years, had simple herpes of the lip before the patient's eruption appeared. The small dose of an elixir of allyl isopropyl barbituric acid was given because the child was restless. I think that he was teething at the time. On one occasion since the eruption began, amidopyrine was administered. Is there any objection to bathing the child, and could potassium permanganate baths be used? I should also like to know of the value of blood transfusions, which have been suggested.

DR. FRED WISE: I think that bathing would be decidedly beneficial. I should give the patients starch baths and bran baths. There is no indication for blood transfusions.

DR. GEORGE M. MACKEE: Blood transfusions have not been found to be of any value in pemphigus.

DR. F. C. COMBES: Would the sedimentation test of the blood be of any aid in arriving at a diagnosis?

DR. R. H. RULISON: Most of the facts in the case have already been covered. I have been wondering whether the application of a dressing to the child's back, something like zinc paste, might be worth while. The child seems to be moving his body constantly in an effort to scratch. An impermeable dressing to prevent contact with the air and the bed clothing might give the child some comfort.

DR. GEORGE M. MACKEE: I suggest that the bullae and the blood be examined for eosinophils and that an iodide test, a sedimentation test and a phytopharmacologic test be made.

DR. HOWARD FOX: When I saw this baby three days ago for the first time I felt as I do now, that I could not do more than call the condition a pemphigoid eruption. As far as the cutaneous lesions are concerned, it is pre-

cisely similar to pemphigus in adults. It was necessary to consider the possibility of extensive impetigo contagiosa, of a bullous eruption following the introduction of a foreign protein and of a drug eruption. Against the diagnosis of impetigo was the fact that no one who came in contact with the patient had this disease and that cultures of fresh bullae, containing clear serum, were sterile. As a therapeutic test, compound solution of copper and zinc sulphate (Alibour's solution) has been used freely for the past two days, with no benefit. The only foreign protein that has been administered was smallpox vaccine, given four months before the eruption began, and the only internal medication consisted of 4 drops of an elixir of allyl isopropyl barbituric acid given about two months before the onset of the eruption. No iodized salt was used by the family. There are no erythematous areas to suggest erythema multiforme, the vesicles and bullae arising on normal skin. There is no objective evidence of the severe itching which occurs in dermatitis herpetiformis. I hesitate to call the condition pemphigus vulgaris because one does not really know the nature of pemphigus. Certain features of pemphigus are lacking, notably the lesions in the mouth. There has been no loss of weight, though the gain in weight has been somewhat below normal for a child of the patient's age. He does not look or act sick in spite of the extent of the eruption. The comparatively little fever that he has had could easily result from secondary infection. I should like to have a Pels-Macht test made, as well as a sedimentation test of the blood. I see no indication for the use of blood transfusions, and my experience with them in pemphigus has been disappointing. Baths would be not only permissible but probably advantageous. An extensive pemphigoid eruption in an infant is the only diagnosis I can make at present. I think that the process is probably benign and that the patient will recover.

URTICARIA PIGMENTOSA? DRUG ERUPTION? Presented by DR. FRED WISE.

H. J., a man aged 21, born in the United States, appeared at the skin clinic of the New York Post-Graduate Medical School and Hospital on Feb. 24, 1934, giving a history of having had an eruption on his back for almost a year.

On the upper part of the back and in the right subaxillary space is a scattered eruption composed of roundish, dark to light brown, slightly raised, smooth papules varying in size from that of a large pinhead to that of a small pea. There is slight elevation of the lesions after irritation by rubbing. The patient does not have any subjective symptoms and seems to be in good health. He says that he has had no internal medication except an occasional dose of phenolphthalein.

A biopsy was done on February 24, but the report has not been received.

NOTE.—The histologic observations failed to reveal the nature of the excised tissue, showing only a banal mild inflammatory process.

DISCUSSION

DR. EUGENE F. TRAUB: I agree with the diagnosis of urticaria pigmentosa.

DR. F. C. COMBES: I agree with the diagnosis. I suggest, however, that instead of using the term "urticaria pigmentosa" one employ the name that Colcott Fox gave the condition, namely, "xanthelasmoidea." "Urticaria pigmentosa" suggests a relationship to urticaria. These lesions, however, are of the nature of nevi and their only similarity to urticaria is that they rise up in wheals on friction.

A CASE FOR DIAGNOSIS (PYODERMIA?). Presented by DR. HANS J. SCHWARTZ.

E. H., a man aged 64, is presented from the clinic of the New York Hospital. The eruption began on the dorsum of the right hand and shortly afterward appeared on the dorsum of the left hand. It began as a small lesion and gradually spread until now the dorsa of both hands are completely covered, extending from the wrists down to and partially involving the dorsal surfaces of the proximal phalanges. The center of each lesion is smooth, and the periphery is distinctly raised and in some places nodular. The lesions are deep purple and at the

periphery apparently purpuric. The patient complains of no subjective sensations. There are no lesions elsewhere on the body. The condition suggests dermatitis medicamentosa of the "fixed" type, but no definite history of drug ingestion has been obtained; this question is being investigated further.

DISCUSSION

DR. GEORGE M. MACKEE: The eruption is suggestive of blastomycosis.

DR. EUGENE F. TRAUB: I showed a number of cases like the present one, also with a doubtful diagnosis, and it was not until Dr. Fox presented a similar case with a diagnosis of vegetating and verrucous pyodermia of the hands of streptococcic or staphylococcic origin that I realized that probably all these cases belong in the same category.

DR. F. C. COMBES: I thought of Dr. Traub's suggestion when I looked at this patient, that is, a staphylostreptococcic infection, such as that described by Gougerot, except that this man has the eruption on both hands. This of course is entirely possible.

DR. H. H. WHITEHOUSE: I think that the condition is a mycotic spreading eruption. Further investigation is necessary to discover what the mycotic agent is.

DR. FRED WISE: Can pellagra be excluded without any hesitation? How would one rule out pellagra?

DR. HOWARD FOX: I do not think that a positive diagnosis can be made from the appearance of the lesions, though it is possible that this is the disease which Gougerot described as a vegetating streptostaphylococcic tuberculoid eruption of the skin, a case of which I showed recently. The fact that the histologic examination showed a simple inflammatory reaction tends to rule out a blastomycetic infection.

DR. HANS J. SCHWARTZ: I am sorry not to be able to present histologic studies in this case. A biopsy specimen was taken two weeks ago, but unfortunately the specimen was too small or was taken from the wrong place. It showed nothing of any significance, simply a chronic inflammatory process. I hoped to have the patient come back to the clinic last week, but he did not come until today. I thought that I should like to have him presented for clinical diagnosis anyway. Another biopsy specimen was removed today.

NOTE.—The second biopsy was reported on by Dr. J. Frank Fraser, as follows: "The specimen consists of two papillary projections of the upper corium and epidermis of a verrucous structure. The corium shows an abnormally large number of greatly dilated blood vessels, filled with laked, highly concentrated blood around which in many places are small collections of round cells, indicating a chronic dermatitis. There is also a margin of polymorphonuclear leukocytes with exudation of serum into the corium, indicating a low grade acute process. In places the blood vessel walls are injured, permitting considerable hemorrhage. The epidermis shows some irregular proliferation and branching of the pegs. The histologic diagnosis is acute repairing dermatitis."

A CASE FOR DIAGNOSIS (TUBERCULOSIS). Presented by DR. EUGENE F. TRAUB.

L. M., a schoolgirl aged 15, was presented at the Nov. 28, 1933, meeting of the society.

DISCUSSION

DR. PAUL BECHET: As Dr. Fox said, one can only guess at the diagnosis by inspection alone. The lesions are sharply defined and rather circinate. I therefore suggest the possibility of eczematized tinea, despite the fact that the toes seem free.

DR. FRED WISE: I cannot disassociate this eruption in my mind from a possible tuberculous process. The age of the patient and the location of the eruption make me think that it is tuberculous. Every effort should be made to

exclude tuberculosis, especially by guinea-pig inoculations, graded tuberculin tests, etc., The patient should be treated with a salt-free diet and rest in bed, as though the condition were known to be tuberculosis. I have no definite diagnosis to offer.

DR. PAUL BECHET: Does Dr. Wise not consider the lesions extremely superficial for those of tuberculosis?

DR. EUGENE F. TRAUB: Dr. Wise asked me before about tuberculin tests. I am sure that some graded tests were made in the beginning, I cannot recall exactly the results but I know that they were not considered unusual. Roentgenographic examination of the chest revealed nothing abnormal, and a medical examination gave negative results. All blood chemistry tests and blood counts, the Wassermann reaction, etc., were normal. I questioned the patient and feel that I have ruled out a drug eruption. An artefact was also thought of, and a sealed dressing was applied to one leg, but the eruption became worse under the dressing and this was discontinued. Nothing seemed to have any prolonged therapeutic benefit with the exception of subcutaneous injections of bacteriophage. These practically cleared up the eruption, but within a short time it recurred.

TUBERCULOSIS OF THE HYPODERM (DARIER-ROUSSY SARCOID?). Presented by DR. F. C. COMBES.

This man, aged 39, a native of Ireland, was admitted to the skin clinic of the New York University Medical College the first week in January 1934, presenting lesions of four months' duration in the following locations: (*a*) the upper part of the right arm near the shoulder; (*b*) the right buttock; (*c*) the posterior portion of the left side of the chest; (*d*) the right thigh (two lesions), and (*e*) the left thigh.

The lesions have appeared spontaneously and vary in diameter from 1 to 4 cm. They are subcutaneous, indurated and adherent to the skin, which cannot be picked up readily with the fingers. Over some of the larger lesions there is some bluish discoloration of the skin, and one or two lesions show slight scaling. The lesion on the back shows some depression without induration, as it is resolving. One lesion on the right thigh shows some depression. There are no subjective symptoms and no clinical evidence of atrophy of the skin. On palpation the lesions feel irregularly lumpy, fairly well circumscribed and rather deep, involving the cutis and subcutaneous tissue. On presentation there is distinct evidence that some of the lesions are undergoing involution.

The family history and personal history are of no significance.

The histologic diagnosis is tuberculosis of the hypoderm resembling Darier-Roussy sarcoid.

DISCUSSION

DR. J. FRANK FRASER: Histologically the picture resembles that of Bazin's disease.

DR. EUGENE F. TRAUB: One of the lesions on the thigh seems clinically to be a characteristic sarcoid of the Darier-Roussy type. On the other hand, the lesions on the buttock differ entirely in appearance and represent either the same condition in a different stage of development or a different entity. I have no suggestions as to the diagnosis of the lesions on the buttock.

DR. H. H. WHITEHOUSE: I am inclined to think that the condition is the Darier-Roussy type of sarcoid. That is backed up by the results of the microscopic examination. Some of the tumors are painless. Some of them appear to be different from others because they are not so near the surface.

DR. FRED WISE: I agree with the diagnosis of the Darier-Roussy type of sarcoid.

DR. HOWARD FOX: The presence of several deep-seated, insensitive, dull reddish nodules with unbroken skin which show a sarcoid structure histologically makes the diagnosis of the presenter most likely.

DR. R. H. RULISON: I agree with the diagnosis of the Darier-Roussy sarcoid.

DR. F. C. COMBES: I think that all of the lesions are the same process. The fact that some of them seem a little more superficial than others does not mean that they are of a different nature. As far as the differentiation between sarcoid and erythema induratum is concerned, I think the differential diagnosis between the two is better made clinically than histologically. Erythema induratum practically always in time breaks down somewhere, and the lesions are of relatively long duration. Some of these lesions in the past six months have disappeared spontaneously without any ulceration. The reason that I called the condition tuberculid rather than tuberculosis is that I hesitate to call it tuberculosis without demonstrating the bacilli either histologically or by guinea-pig inoculations. The histologic section showed the classic picture of tuberculosis.

DR. J. FRANK FRASER: I did not mean to convey the impression that I think that the patient has Bazin's disease (erythema induratum), but when I looked at the slide I was impressed with the resemblance to that condition.

A CASE FOR DIAGNOSIS. (ERYTHROPLASIA OF QUEYRAT?). Presented by DR. HANS J. SCHWARTZ.

J. C., a physician aged 31, first noticed the lesion which he presents toward the end of November 1933. It began in the sulcus and gradually spread backward over the shaft of the penis and forward over the glans for about 1 cm. in each direction. There has never been any exudation. Slight itching has been noted at times. The patient first came under my observation early in December 1933, and there has been practically no change in the appearance of the lesion since that time.

There is a superficial inflammatory lesion on the dorsum of the penis about 2 cm. in width and extending about 1 cm. back from the sulcus and the same distance forward over the glans penis. The surface is dry and shows slight scaling. Little or no infiltration can be felt. The border is sharply demarcated but not appreciably raised. Repeated dark-field examinations and Wassermann tests have been negative. There is no history of drug ingestion.

A biopsy was performed, and the report by Dr. J. Frank Fraser was as follows: "There are changes in both the epidermis and the corium. In the epidermis the chief histologic signs of a malignant process, such as hyperchromatism of the nuclei, mitotic figures and lymphatic invasion, are absent. The changes present are a moderate amount of edema, some disturbance of polarity, hyperplasia of the prickle cell layer and a tendency to disruption of the basal layer. The corium shows dilated capillary vessels, around which in places is a mild degree of round cell exudation. The collagen bundles show a tendency to fibrosis and hyalinization. It seems impossible from the histologic picture to determine the sequence of these alterations, in other words, whether the changes in the epidermis or those in the corium are primary."

The case is presented primarily for diagnosis, but the diagnosis of erythroplasia of Queyrat is suggested for consideration.

DISCUSSION

DR. HANS J. SCHWARTZ: I shall be much indebted to the members if they will give me suggestions not only as to diagnosis but particularly in regard to treatment.

DR. FRED WISE: I think that the condition is erythroplasia and should be treated with one thorough application of monopolar desiccation.

DR. JEROME KINGSBURY: As far as the treatment is concerned, the important thing is not to do too much. I think that this is a case for continued observation rather than for vigorous or radical treatment at the present time.

DR. J. J. ELLER: I have seen only two patients with erythroplasia. One was under observation at the clinic for six or eight months. I was under the impression

that the lesions have a moist surface in most cases. This patient's lesions are dry most of the time, and against the history of erythroplasia is the fact that he said that some of the individual lesions disappeared or became smaller on one edge of the patch without treatment. I should be inclined to handle the case as Dr. Kingsbury suggested, that is, to keep the patient under observation a little longer, with palliative and conservative treatment, to see whether the condition may be lichen planus or some other benign eruption, not a premalignant one.

DR. H. H. WHITEHOUSE: I agree with the last two speakers. I do not advocate drastic treatment. I should make further observations and wait longer before applying electrodesiccation.

DR. F. C. COMBES: In view of the fact that the histopathologic picture is definitely that of erythroplasia and eliminates lichen planus or any other simple dermatosis, I think the more radical treatment suggested by Dr. Wise is the proper procedure.

DR. J. FRANK FRASER: I have not had the opportunity to study any cases of erythroplasia, but if the histologic picture and the gross appearance are what one usually finds in that condition, Dr. Schwartz is justified in presenting the case as an example of that disease. I disagree with Dr. Kingsbury's view that the lesion should not be treated and agree with Dr. Wise that electrodesiccation is indicated.

DR. GEORGE M. MACKEE: Erythroplasia is not well known either clinically or histologically. The cases in the literature as well as the three or four that I have studied have shown clinical variations. The lesion may be dry, but there is usually some exudation which may be copious. Apparently the disease may simulate, in the early stage, the inflammatory dermatoses, such as psoriasis and eczema. The lesion is usually well marginated. Histologically, this patient's condition does not appear to be inflammatory. It seems to be neoplastic. The process is in the epidermis. The basal layer is disorganized. The edema is intracellular. There is interference with the nuclei. In other words, there appears to be beginning anaplasia. Therefore, I think that both clinically and histologically the condition is erythroplasia.

Erythroplasia is exceedingly stubborn. Apparently there is no treatment that is entirely successful. It does not respond satisfactorily to roentgen rays or radium; even vigorous electrocoagulation fails to cure it in some cases. The main point, however, is that nearly every case of erythroplasia that has been followed through has eventuated in carcinoma. Whether the condition is precancerous in the beginning or true cancer is under controversy. Therefore, while it might be safe to keep this patient under observation for a little while to establish definitely the diagnosis of erythroplasia, I should not wait too long. Electrocoagulation is perhaps the best treatment.

DR. R. H. RULISON: I think that regardless of the exact diagnosis, on the basis of Dr. Fraser's and Dr. MacKee's observations under the microscope, the lesion merits thorough destruction.

DR. HOWARD FOX: Before attention was drawn to this peculiar disease, erythroplasia, I think that all dermatologists must have seen plaques somewhat like this one on the glans penis or on the sulcus which they were apt to call psoriasis, seborrheic eczema or possibly lichen planus. The condition was considered to be a harmless inflammatory disease. The microscopic observations have apparently ruled out simple inflammation in this case. It seems to me also that five roentgen treatments without any improvement tend to exclude simple inflammation. I think that erythroplasia is the probable diagnosis and that Dr. Wise's suggestions for treatment are reasonable.

DR. HANS J. SCHWARTZ: I am much indebted to the members for this discussion. This is an important case for the patient. I too feel that one must not temporize long. I am inclined to watch him a little longer and perhaps have more sections made and study them more carefully. The first ones made were not very satisfactory. I will report to him tomorrow the opinion of the members.

The majority seem to think that the case should be handled drastically. In regard to exudation, the lesion has not shown any real exudation while under my observation. When the patient first came to me there was something suggesting crusting on the corona. When that was removed there was little if any moisture underneath.

REPORT ON A CASE PRESENTED FOR DIAGNOSIS AT THE JAN. 23, 1934, MEETING. Presented by DR. GEORGE M. MACKEE.

At the last meeting I presented a priest who had an eruption on the side of the neck with sinuses and ulcers. The case was investigated thoroughly, and it turned out to be one of streptococcic cellulitis and lymphangitis. Shortly after the last meeting erysipelas developed, which cleared up under the influence of antitoxin treatment. He is now improving satisfactorily with continuous application of wet dressings.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILOLOGY

EUGENE F. TRAUB, M.D., *Secretary*

March 6, 1934

LEO SPIEGEL, M.D., *Chairman*

LATE SECONDARY SYPHILIS. Presented by DR. A. BENSON CANNON.

This white man, aged 41, was admitted to the City Hospital on Jan. 1, 1934, complaining of nonpainful and nonitching lesions on the face, arms and legs of one month's duration. The lesions started as small papules, some of which disappeared after two weeks while others became pustular and dried up, leaving a white, thick scale. Two months prior to admission the patient was treated for buboes on the right side. He denied having had a chancre or any urethral discharge.

At the present time, on the center of the forehead there is a group of fleshy red papules covering an area 5 by 4 cm. Some of the lesions have coalesced and are covered with a thick, white scale. On each cheek, touching the nasolabial line, there is an irregular, dollar-sized area bordered by papular and scaly lesions. The center of the area appears to be atrophic. Over both elbows there are grouped pea-sized papules covered with a thick, white, micaceous-like scale. There are several dollar-sized lesions covered with the same type of scale on the extensor surface of each arm, and two or three dime-sized lesions with depressed, crusting scales. The lesions extend down the extensor surfaces of the arms and include the backs of the hands. There was formerly one dollar-sized lesion on the back of the left leg, which has healed, leaving only a pigmented area; but smaller, scaly lesions about the site are still present, as well as a scattering of pinhead-sized papules down the extensor surface of the legs.

The Wassermann reaction of the blood was 4 plus. The reaction of the spinal fluid was negative. The patient has received one course of silver arsphenamine and two injections of mercuric salicylate. Some improvement of the lesions has resulted, especially in those of the face. The patient is presented to show the marked resemblance to psoriasis.

DISCUSSION

DR. ISIDORE ROSEN: This case is interesting because of the close resemblance of the eruption to psoriasis. I have seen a number of patients with annular psoriatic lesions which resembled syphilis, but I have never seen such characteristic psoriatic scales in secondary syphilis.

DR. ADOLPH ROSTENBERG: I have seen lesions of secondary syphilis assume a psoriatic appearance in a case in which the patient had previously had psoriasis. The lesions on this patient's forearms closely resemble psoriasis and might be called secondary syphilis; but the circinate lesions on the forehead look like tertiary lesions.

DR. E. WILLIAM ABRAMOWITZ: The lesions on the face resemble more the rosacea type of nodular tertiary syphilis. The lesions on the arms might be mistaken for psoriasis except that they are more infiltrated and annular. I have recently encountered two patients with psoriasiform syphilis, the lesions having appeared in spite of treatment with arsphenamine.

DR. A. BENSON CANNON: While this patient has some lesions that are typical of late secondary syphilis, others resemble psoriasis, and still others, lichen planus; and there are some on the cheeks that have been mistaken for lupus erythematosus. The Wassermann reaction was strongly positive, and the lesions have improved under antisyphilitic treatment.

TUBERCULOSIS? GRANULOMA INGUINALE? Presented by DR. A. BENSON CANNON.

This colored man, aged 30, was admitted to the City Hospital on Nov. 19, 1933, with an ulceration of the scrotum and intergluteal region. In October 1933 a chafing of the sides of the scrotum and intergluteal region developed, and the area became infected, causing considerable swelling. Several hard masses developed, which later broke down and discharged. Similar discharging lesions developed in the inguinal region.

The entire scrotum is now red and edematous, and on its lateral surfaces are several bean-sized, raised, granular lesions from which pus exudes. Other lesions show ulcerations with granular bases. Along the surface are several granular openings exuding pus. There are several healing lesions in the right inguinal area.

Proctoscopic examination of the lower part of the rectum revealed normal tissue. A large abscess with multiple openings was noted in the perineal tissue.

The Wassermann reaction of the blood was repeatedly negative, as were also the reaction of the spinal fluid, smears for Donovan bodies and the Frei test.

The patient has received fifteen injections of sodium antimony thioglycollate and ten injections of silver arsphenamine. There has been no improvement.

DISCUSSION

DR. DAVID BLOOM: I have two similar male patients under my observation at Bellevue Hospital in the service of Dr. Howard Fox. For several years each has had large masses around the anus, with ulceration and involvement of the rectum. One of them presents marked elephantiasis of the scrotum and destruction of the anus with incontinence of feces. The Frei test was negative. Donovan bodies were not found, and a biopsy showed simple inflammation. The result of the guinea-pig inoculation has not been reported. One of the patients has been receiving antimony and potassium tartrate and has improved considerably. I doubt if the diagnosis of granuloma inguinale in such cases is justified in the event that the lesions respond to antimony and potassium tartrate, for this drug seems to have a favorable influence on many diseases. The etiology of this condition has still to be considered obscure.

PARAPSORIASIS EN PLAQUES. Presented by DR. ISIDORE ROSEN.

This white man, aged 40, born in Russia, first came to the clinic of the New York Post-Graduate Medical School and Hospital on Feb. 21, 1934, with a generalized eruption consisting of erythematous, scaly plaques, varying in size from that of a pea to that of a silver quarter. The lesions are most marked on the trunk and on the face. Many of them are confluent, forming larger plaques. The larger lesions are somewhat infiltrated. The lesions on the face are more

infiltrated and more erythematous than those on the trunk. Some of them have adherent scales. The soles are covered by thick hyperkeratoses with fissures. There is no evidence of scarring or of atrophy, nor are there areas of alopecia on the scalp. Palmar lesions are absent. There is some pruritus. The patient received four roentgen treatments elsewhere.

The blood count showed a hemoglobin content of 94 per cent, 4,600,000 red cells and 7,800 white cells, with 50 per cent polymorphonuclears, 5 per cent eosinophils, 1 per cent basophils, 1 per cent mononuclears and 43 per cent lymphocytes. The Wassermann reaction of the blood was negative. Biopsy showed retrogressing or quiescent parapsoriasis.

DISCUSSION

DR. ABRAHAM WALZER: This patient was under observation by my associates and me for six months. He presented typical psoriasis. The only objection to the diagnosis was the peculiar configuration. Gradually we inclined toward the diagnosis of parapsoriasis. When the lesions were first seen, we thought of mycosis fungoides. The itching was more pronounced.

DR. HERMANN FEIT: How many cases of parapsoriasis develop into mycosis fungoides? Can parapsoriasis be definitely diagnosed histologically?

DR. GEORGE C. ANDREWS: I think that the diagnosis cannot be made by clinical examination. It can be made only by a study of the further course of the disease unless some definite histologic observations clinch the matter.

DR. SIGMUND POLLITZER: Eruptions that look like parapsoriasis en plaques prove to be mycosis fungoides in a certain percentage of cases. It is often impossible to differentiate the two conditions clinically, and only exceptionally does histologic examination help. It is interesting to recall that of the two cases described in 1890 in the paper by Unna, Santi and me, which introduced the group of diseases later labeled "parapsoriasis" by Brocq in 1902, one proved later to be an instance of mycosis fungoides. Similar mistakes in diagnosis have repeatedly been made and seem to be unavoidable. It is enough to have in mind the possibility that an early case of parapsoriasis en plaques may turn out to be a much more serious condition.

DR. FRED WISE: The literature mentions several instances in which the diagnosis of parapsoriasis en plaques was made in the earlier stages of the eruption and changed later to mycosis fungoides. In the case of Dr. F. of New Jersey, formerly a patient of Dr. Pollitzer and myself, the parapsoriasis persisted for from twenty to twenty-five years, and at the time of the patient's death from nephritis there was no evidence of mycosis fungoides. I believe that the eruption presented by Dr. Rosen's patient is psoriasis rather than parapsoriasis.

DR. ISIDORE ROSEN: This patient has not been under observation long enough for all investigations to be made, but there are a number of unusual clinical features which make the diagnosis difficult. The lesions on the face and scalp suggest psoriasis; those on the trunk, parapsoriasis or mycosis fungoides. The lesions on the trunk, especially on the back, show the unusual configuration which is sometimes seen in the erythematous stage of mycosis fungoides, and yet the pale superficial lesions with thin scales on the flanks are characteristic of parapsoriasis and unlike mycosis fungoides.

MORPHEA WITH XANTHOMATOUS INFILTRATION. Presented by DR. PAUL GROSS.

This woman, aged 32, about one and one-half years ago, shortly after she had stopped thyroid medication for a dry condition of the skin, noticed a few purple spots on the left leg. Similar lesions appeared later on both thighs and finally on the right leg. None of these spots have disappeared. She noticed that a few months ago the central portion of the lesion on the left leg had become yellow. There has been no pain, itching or tenderness.

On the anterior surface of the left leg there is a large infiltrated plaque with a purplish border and central atrophy. Portions of this atrophic area show

orange-yellowish discoloration and an increase in substance. The lesions on the thighs are smaller but show a similar condition. On the right leg are small purplish macular lesions.

Examination of the blood showed 0.91 Gm. of sugar per liter, 0.28 Gm. of urea per liter and 173 mg. of cholesterol per hundred cubic centimeters. The urine contained no sugar or albumin.

Biopsy revealed a granular layer which was thin but definite. There was moderate edema. Little melanin was present. The corium showed marked changes. It was quite cellular, the collagen showed evidence of degeneration and some of the bundles were swollen and hyalinized. The blood vessels seemed to be increased in number. There was a marked infiltration of cells about them and about the coil gland acini. Numerous large vacuolated, often multinuclear cells were seen both in the superficial corium and forming nodules in the deep corium in the neighborhood of the hypoderm. The blood vessel walls showed thickening. The endothelium was often swollen. The fibroblasts were swollen and increased in number, and many cells were present which resembled lymphocytes. Larger mononuclear cells, some of them granular, were noted. The large cells and multinucleated giant cells seemed to contain droplets. Round hyaline bodies were seen, some of these within cells. A great many large droplet-filled cells were seen where the collagen had degenerated and was being phagocytosed. Slides stained with scarlet red showed collections of fat in the infiltrated portions of the corium. Fat seemed to be situated also between the collagen fibers and contained in cells. A frozen section seemed to indicate that the collagen was swollen. There was no doubt of the xanthomatous degeneration of the skin; there was some doubt on histologic grounds of the true sclerodermatous nature of the lesion. The histologic diagnosis was xanthomatous degeneration of the skin.

DISCUSSION

DR. OSCAR LEVIN: I offer the diagnosis of sarcoid.

DR. T. J. RIORDAN: In a recent report of a case of necrobiosis lipoidica diabeticorum, Zeisler and Caro of Chicago described plaques with a peripheral yellowish discoloration and a deeper central discoloration. In this case the lesion shows just the reverse, namely, violaceous periphery and a center xanthoma-like in color.

DR. PAUL GROSS: The diagnosis of sarcoid was considered, in addition to that of morphea, but the clinical picture seemed to be in favor of the latter. The fully developed lesion shows clearly a purplish, slightly infiltrated border and a whitish, smooth, apparently atrophic center. The unusual feature is the yellowish infiltration within the atrophic area. This clinically suggested a xanthomatous degeneration, and histologically that assumption was proved to be true. Since it is known that xanthomatous formation may occur in scars and atrophy (Dr. Harris presented a patient a few years ago with xanthoma in a scar from tertiary syphilis) this factor seemed to indicate that the patient under discussion has a disease characterized by degenerative changes in the connective tissue. A biopsy specimen taken from the whitish center of a lesion would probably show the characteristics of scleroderma better than the one taken from the more inflammatory border.

DR. SIGMUND POLLITZER: I saw no xanthoma cells in the section. On the other hand, there was a fair amount of scattered particles in the upper cutis that took the scarlet red stain. I suggest as a diagnosis lipid infiltration rather than xanthoma.

PSORIASIS OF THE MUCOCUTANEOUS SURFACE AND VERMILION OF THE LIPS. Presented by DR. HERMANN FEIT.

This youth, aged 17, has never been seriously ill. His skin disease started about ten years ago and has disappeared, as a rule, during January, February,

March and April. This year, however, it has continued and for the first time has appeared on the lip. There is no history that any other member of the family has had a similar condition. The patient's skin tans easily but never blisters after exposure to the sun. The mucous membrane of the lips on the mucocutaneous surface and the rest of the covering show dry, micaceous scaling similar to that on the skin, which also shows capillary bleeding. The lips are fissured and bleed easily. The mucous membrane of the lip desquamates in rather large flakes. The scalp, face, legs and arms show typical psoriasis. The nails appear to be normal.

SYPHILIS WITH CHARCOT'S KNEE JOINT. Presented by DR. A. BENSON CANNON.

This man, aged 52, a German, was admitted to the City Hospital on June 20, 1933, because of severe swelling, redness and tenderness of the left knee of two months' duration, which developed about one day after an injection of arsphenamine. The patient had gonorrhea and a chancre twelve years ago and received ten injections into the hip at that time. He had received no treatment since until the injection just mentioned was given. During the past ten years he has had recurring lesions on the legs, thighs, arms and face, which he described as "boils," which left scars. The leg has been in a cast for six months, and mercury and iodides have been given, with gradual diminution of the swelling and pain.

There is now irregular, patchy, atrophic scarring with some loss of deeper tissues on the right leg, extending from above the knee to the foot. A similar type of scarring involves the lower part of the left thigh and the upper half of the leg. Many smaller scars, varying in diameter from that of a pea to that of a dime, are present on the forehead, neck, arms and shoulders.

Roentgen examination of the left knee joint at the time of admission showed a marked diminution in the joint space. There were hypertrophic changes involving the posterior aspect of the lower end of the left femur and the upper end of the left tibia. There was marked swelling of the soft tissue about the joint. The patella seemed to be floating as though there was fluid beneath it and the lower end of the femur.

The Wassermann reaction of the blood on three occasions was 4 plus. The reaction of the spinal fluid was 4 plus with 0.2 cc. and 3 plus with 0.1 cc. of fluid.

The colloidal gold count was 1111110000. The patient has received potassium permanganate dressings and mercury.

The redness and tenderness have disappeared, and the size of the knee joint has greatly diminished. The patient cannot stand on the affected leg. He was presented to show also extensive scarring from syphilis.

CHANCROID. Presented by DR. A. BENSON CANNON.

C. R., a white man, aged 30, was admitted to the City Hospital one week ago with an ulcer of the penis of six weeks' duration. The lesion began on the prepuce and was treated by the family doctor with local remedies. Three weeks ago that physician removed the lesion with an electrocautery, after which the ulceration spread. The patient had a chancre and a 3 plus Wassermann reaction one year ago. He received two courses of injections into the arm and two into the hip.

There is an irregularly shaped, superficial, necrotic ulceration with a yellowish slough over the base and irregular ragged beveled edges, measuring 1¼ by ¾ inches (3.1 by 1.9 cm.) in its largest diameter, and involving the left half of the dorsum of the glans penis. On the corona, just to the left of this, is a similar pea-sized area. The whole prepuce is swollen and moderately hard, and the lateral and dorsal sides are occupied by similar necrotic ulcerations. A portion of this ulcer has infiltrated and rolled borders. The anterior surface of the prepuce presents a pendulous mass. There is bilateral inguinal adenopathy, the glands being almond-sized and nontender. There is no skin rash, pharyngitis or alopecia. Dark-field examination and the Wassermann test gave negative results. The Ducrey bacillus was demonstrated.

LUPUS VULGARIS: ACQUIRED HYPOSPADIAS. Presented by DR. A. BENSON CANNON.

This white man, aged 53, a glassworker, was first admitted to the City Hospital in 1910, with a chancre and a positive Wassermann reaction. After four injections of arsphenamine his Wassermann reaction became negative, but a dermatitis appeared on the thighs. During the second course of arsphenamine the dermatitis was much aggravated. The chancre healed, with an acquired hypospadia. From then until 1924 the patient was treated at intervals at various hospitals and received a total of fourteen injections of arsphenamine and many of mercury, as well as numerous x-ray and ultraviolet ray treatments. There has been a gradual extension of the condition from the buttocks to below the knees.

The patient was readmitted to the City Hospital in 1924, where a biopsy on the lesions and inoculation of material into a guinea-pig showed the condition to be tuberculous. The lesions were curetted and desiccated as much as possible without general anesthesia, which was inadvisable because of a heart lesion. The treated areas healed with scar formation, but the eruption spread to the legs. Both blood and the spinal fluid gave negative reactions.

The patient was again readmitted to the City Hospital in September 1933, at which time he showed healed lesions of lupus vulgaris. These lesions now extend from the torso to the lower third of the right leg and to the ankle of the left leg, with ten or twelve punched-out ulcers with granular bases and covered with a dirty exudate which vary in size from that of a twenty-five cent piece to that of a half dollar. The entire area shows smooth, red keloidal scars, some with verrucous thickenings. In the groins and on the trunk are several areas of telangiectasia in the scarring, which are probably the result of x-ray therapy.

The urine was normal, and the Wassermann reaction of the blood was negative. The blood count was normal.

The patient is presented to show extensive scarring and ulcers resulting from tuberculosis cutis.

MANHATTAN DERMATOLOGIC SOCIETY

MIHRAN B. PAROUNAGIAN, M. D., *Secretary*

March 13, 1934

HOWARD FOX, M.D., *Chairman*

LYMPHOBLASTOMA OF THE SCALP. Presented by DR. GEORGE C. ANDREWS.

O. W., a man aged 34, was presented at the February 1934 meeting of this society. Since that time a roentgenogram of the skull has been made, which showed no changes in the bony structures but some swelling of the soft tissue. These findings indicate that the firm mass on the left side of the back of the neck was a swollen gland and not a neoplasm of the skull. A biopsy has been made, which showed the lesion to be a lymphoblastoma. The cytologic characteristics were not sufficiently determinate to make it possible to classify the type of growth exactly. The histologic picture suggested leukemia, Hodgkin's disease or mycosis fungoides. Another biopsy will be made and special stains used.

The blood count was as follows: hemoglobin, 122 per cent; erythrocytes, 6,300,000; leukocytes, 11,400; platelets, 186,000; neutrophils, 46 per cent; eosinophils, 3 per cent; basophils, 1 per cent; mononuclears, 9 per cent, and lymphocytes, 41 per cent.

The tumors of the scalp were treated with one-half erythema dose of unfiltered roentgen rays (140 roentgens) two weeks ago and have disappeared, although erythematous patches remain at their sites.

DISCUSSION

DR. J. FRANK FRASER: I wish to repeat what I said in opening the discussion on this case at the February meeting, that the condition is one of the lymphoblastomas, either mycosis fungoides d'emblée or a reticular cell lymphosarcoma. It is probably not Hodgkin's disease, as that condition is very rare in the skin. I have not seen the slides.

DR. DAVID L. SATENSTEIN: I get the impression that the condition is not mycosis fungoides. I still favor the opinion advanced at the previous presentation. The history, the clinical appearance and the clinical course are in favor of a Spiegler-Fendt sarcoid. The microscopic observations tend to corroborate that diagnosis.

DR. FRED WISE: Basing my opinion on cases which I have seen before, I should say that the patient has leukemia of the skin, not Hodgkin's disease and not mycosis fungoides. It is possible to have a lesion like this without characteristic blood changes, as in aleukemia and subleukemia of Arndt.

DR. LUDWIG OULMANN: The patient gave a history of having the condition disappear previously without any treatment. In connection with the changes in the blood picture, this speaks more for a disturbance of the blood than for a tumor formation such as Hodgkin's disease.

DR. LOUIS B. MOUNT: It certainly is not normal to have a blood picture such as this man has. It indicates that the condition belongs to the leukemic group.

DR. GEORGE C. ANDREWS: I shall follow the case further and have more blood counts made and go into the history as to diabetes, which may have a bearing on the condition. My impression agrees with that of Dr. Wise, and I favor a leukemic condition rather than Hodgkin's disease.

DR. FRED WISE: Does polycythemia have any characteristic cutaneous manifestations?

DR. PAUL E. BECHET: In answer to Dr. Wise's question, I had under observation recently a patient with typical polycythemia whose hands were of a dark, livid color. The face also presented a bluish, dark red rosacea-like appearance. Venules were apparent in the skin of the nose.

DERMATITIS HERPETIFORMIS; EPITHELIOMA. Presented by DR. MIHRAN B. PAROUNAGIAN.

B. B., a man aged 70, first appeared at the skin clinic of Bellevue Hospital in October 1931, with a history of an extensive rash on the body of about eight months' duration. The rash began on the left leg and spread to the body, always being very itchy. Twice, while under treatment, the eruption has cleared up entirely and has remained absent each time for a few months.

The lesions consist of erythematous vesicles chiefly, with a few papular lesions interspersed, grouped in smaller and larger clusters, on the arms, in the axillae, in the lumbar region and over the sacrum and the posterior aspects of the thighs. The Wassermann test was negative. The urine showed a faint trace of albumin but no sugar. The blood count was as follows: hemoglobin, 95 per cent; red cells, 5,050,000; white cells, 7,250; polymorphonuclears, 66 per cent; lymphocytes, 28 per cent, and eosinophils, 6 per cent.

The patient has received many kinds of external and internal therapy, including arsenic, calcium, sodium thiosulphate, autohemotherapy, etc.

The lesion on the nose has been present about eight years. It is a small, solid, skin-colored, raised lesion, centrally depressed and with a definite shiny border; it shows a small scale.

DISCUSSION

DR. FRED WISE: I agree with the diagnosis as presented. There is no pigmentation, but I assume that pigmentary changes may occur later.

DR. LOUIS B. MOUNT: The members may recall that at one of the meetings I presented a man with a grouped, constantly recurring macular eruption of Duhring's disease of several years' duration, and the only one who had seen a case like that was Dr. George Henry Fox. There was never a papular or vesicular lesion.

DR. GEORGE C. ANDREWS: The point that impressed me about this patient was the filthy condition of his teeth. I think that they may be a source of infection, possibly one of some importance.

DR. PAUL E. BECHET: Duhring, in his original monographs, particularly dwelt on the polymorphic appearance of the disease, and he clearly described the many faceted lesions which this disease so frequently presents.

DR. HOWARD FOX: In the usual description of Duhring's disease there are mentioned four cardinal features: polymorphism, grouping, itching and a tendency to relapse. This patient showed only two of these, namely itching (which was severe) and grouping. I think that the condition should be classed as dermatitis herpetiformis. Three procedures are of some value in making the diagnosis of that disease, namely, the potassium iodide test, the sedimentation test of the blood and the eosinophil count.

DERMATITIS ARTEFACTA. Presented by DR. MIHRAN B. PAROUNAGIAN.

J. B., a man aged 48, visited the Lincoln Hospital in May 1932 because of a small sore on the right hand. His Wassermann reaction was 4 plus. He was given eighteen injections into the arm and the same number into the hip. He had never had a chancre but had gonorrhea thirty years ago. In 1923 he received sixteen injections into the arm and sixteen into the hip.

While under treatment at the Lincoln Hospital, an itching eruption developed on the back from which persistent sores developed.

In December 1932 he went to the Stuyvesant Square Hospital because of the persistent sores. The Wassermann test of his blood was negative, but he was found to have diabetes. A biopsy was made (the report on which is not known). For the diabetes, he received 75 units of insulin twice weekly and was given a special diet. This was continued for about seven months, but there was no improvement in the cutaneous condition. In fact, new lesions appeared from time to time.

He came to the skin clinic at Bellevue Hospital in July 1933, at which time his Wassermann reaction was persistently negative. The lesions were grouped, being present on the outer aspects of both upper arms and forearms, over both scapulas and sacrums and on the buttocks, the inner aspects of the thighs and the calves of the legs, with a few on the abdomen and hands. They consisted of superficial circinate and bean-shaped, crusted lesions, showing peripheral healing tendencies and brownish pigmentation marginally. The healed lesions resembled healed burns, with superficial scarring, brownish pigmentation of variable intensity and prominence of the follicles.

The blood sugar was 300 mg. per hundred cubic centimeters on March 5, 1934. The urine sugar was 4 per cent on March 6.

He has received treatment with boric acid ointment, with considerable improvement. The lesions are undoubtedly traumatic.

DISCUSSION

DR. PAUL E. BECHET: I agree with the diagnosis.

DR. DAVID L. SATENSTEIN: I doubt very much whether these lesions were produced by the fingers alone. I am willing to accept the clinical diagnosis, but I am not willing to accept the theory of the agent which produced the lesions.

DR. MAX SCHEER: I believe that some chemical agent was used, rather than simply scratching.

DR. ANDREW J. GILMOUR: I agree with Dr. Satenstein and Dr. Scheer. There are undoubted evidences of the use of acid on the back.

DR. ISADORE ROSEN: The man has a blood sugar of 300 mg. per hundred cubic centimeters. It is known that patients with diabetes who have ulcers are usually very sick. If these ulcerations had been produced by the nails, I feel that the infections would be severer. I believe that the man is using acid, as a caustic.

DR. HOWARD FOX: There is no doubt in my mind that these lesions are self-inflicted, but whether they are produced by scratching or by the application of some escharotic is more difficult to say. There are two features which are unusual in a feigned eruption: first, the almost exact symmetry, and, second, the location of the lesions on the upper part of the back, which is somewhat difficult to reach with the hands.

I might add that, in answer to a question of mine as to whether he is right-handed or left-handed, the patient explained that he is ambidextrous. The appearance of the coin-sized cicatricial patches is not that which is ordinarily caused by scratching. Possibly the presence of diabetes accounts for the susceptibility of the skin to secondary infection and for the formation of these large scars. In my opinion, it is probable that the patient used some escharotic rather than the fingernails. I once showed a patient with a symmetrical eruption of the back which strongly suggested indurated acne. The patient, however, was a drug addict and demonstrated the method by which he introduced a needle into the upper part of his back.

DR. MIHRAN B. PAROUNAGIAN: I hardly think that a caustic was applied, because if it had been, since the patient is diabetic, he would be in danger of gangrene. I have observed the patient scratching himself with his nails and producing these lesions.

LEUKOPLAKIA. Presented by DR. MIHRAN B. PAROUNAGIAN.

G. M., a man aged 57, had a chancre thirty-six years ago and received no injection therapy until he entered the Bellevue Hospital clinic in July 1930. At that time he presented himself because of soreness of the mouth and tongue, and examination revealed leukoplakia and cracking and ulceration of the anterior portion of the tongue. Despite therapy the Wassermann reaction of his blood has always been 4 plus. During the four years at this clinic, he has received sixteen injections of neoarsphenamine, twelve of silver arsphenamine, twenty-two of bismuth sodium gluconate and forty-five of mercuric salicylate injections and a considerable amount of potassium iodide by mouth.

The soreness and some of the lesions disappeared after treatment was begun, but there has been only slight improvement in the leukoplakia. The object of this presentation is to show that the considerable amount of arsenicals employed have not caused a neoplasm.

DISCUSSION

DR. MAX SCHEER: From time to time this question has arisen, and a number of physicians have opposed the use of arsenical treatment for syphilitic patients with leukoplakia. I do not think that leukoplakia is likely to develop into cancer as a result of arsenicals alone; it does not do so unless stomatitis results from the arsenical or other medication.

DR. DAVID L. SATENSTEIN: I believe that in a case presenting simple leukoplakia with no evidence of leukokeratosis and no fissures, erosions or ulcerations, arsenicals may be used. Arsenicals may stimulate epithelial growth when such growth is present before the therapy is begun.

DR. LUDWIG OULMANN: I certainly have seen arsenical dermatitis of the palms and soles after arsphenamine medication. The changes in leukoplakia of the tongue are individually different. I have seen leukoplakia in a patient with a positive Wassermann reaction who had a smooth ulcer at the side of the tip of the tongue. A biopsy was made, which proved the small ulcer to be carcinoma. Not-

withstanding the advice that the lesion be operated on, the patient insisted on arsphenamine treatment and postponed the operation. Six months later the patient died from carcinomatosis.

DR. FRED WISE: In cases of leukoplakia associated with advanced leukokeratosis and evidence of breaking down of tissue, I am convinced that arsenical medication should be avoided, in order to retard the hastening of malignant degeneration of diseased cells.

DR. HOWARD FOX: In my opinion, it is entirely proper to treat syphilis with arsphenamine even when leukoplakia is present, provided there are no fissures, ulcers or nodules or other evidences of carcinoma. Moderna, an Italian who wrote an excellent monograph on leukoplakia buccalis, treats this disease with radium plus injections of arsphenamine.

DR. MIHRAN B. PAROUNAGIAN: I could show six or eight cases of leukoplakia in syphilitic patients who have been treated. I believe that patients with syphilis who have never been treated should be treated. This man's condition was at least 50 per cent worse than it is now. Evidently there is no harm done by arsenical therapy as far as the leukoplakia is concerned.

A CASE FOR DIAGNOSIS (SYPHILIS?). Presented by DR. MIHRAN B. PAROUNAGIAN.

This case was presented at the January and February 1934 meetings of this society. The results of Wassermann tests were as follows: Dec. 11, 1933, negative; December 18, negative; Jan. 10, 17, 22 and 29, 1934, plus-minus; February 5, negative. Injections of silver arsphenamine (0.15 Gm.) were given on Dec. 29, 1933, and Jan. 3, 17 and 31, 1934.

The primary lesion on the glans penis has improved only slightly, and papular lesions have developed on the prepuce. The patient states that the rheumatic pains he had previously have disappeared, and that in general he feels much better.

On February 14, the Wassermann test gave the following results: alcoholic antigen, 3 plus; cholesterol antigen, 4 plus. On February 26, the Wassermann reaction was 4 plus.

At the previous meetings various opinions as to diagnosis were expressed, namely, that the condition was "tuberculosis," "gumma," "chancre redux," etc. There has been no secondary eruption of any sort except a few papular lesions at the prepuce. My diagnosis is chancre; the eleven injections into the hip which he received prior to his admission probably delayed the serologic reactions and the secondary manifestations.

DISCUSSION

DR. ISADORE ROSEN: I still adhere to my original diagnosis of tertiary syphilis. The lesion is markedly improved although the patient has not had much antisyphilitic therapy.

DR. LOUIS B. MOUNT: I agree with Dr. Rosen. I cannot see how a primary lesion could have been present for six months without any glandular involvement. I think that the lesion is tertiary.

DR. GEORGE C. ANDREWS: I think that the lesion is a keloidal scar forming on a syphilitic lesion. Whether the lesion is of primary or of tertiary syphilis I cannot make up my mind.

DR. DAVID L. SATENSTEIN: I am not so ready to accept the diagnosis of a primary lesion. I suggest the possibility of some other condition in a person with a positive Wassermann reaction. Further investigation is necessary before a positive diagnosis can be established.

DR. FRED WISE: I agree with Dr. Satenstein that a great deal more work must be done to identify this lesion, which I now believe is probably syphilitic.

DR. HOWARD FOX: I doubt whether this is an initial lesion, on account of the long duration and the entire lack of local adenopathy. It is also not a clearly tertiary lesion (nodule), as the healing has been slow and the scarring is not of

the type which follows the involution of late lesions. I suggest that part or all of the affected tissue be excised for histologic examination.

DR. MIHRAN B. PAROUNAGIAN: I do not agree with the diagnosis of tertiary syphilis. In the first place, there is no history of a previous infection. There is a history of exposure to infection followed by this sore in two weeks. There are no enlarged glands. He received injections prior to coming to this clinic. If this were a tertiary lesion, one-half the amount of treatment he received would have cleared it up. My associates and I waited to treat him until he got over the effects of the treatment received before coming to us. The fact that his Wassermann reaction became gradually positive after the effects of the previous treatment passed off makes me consider the lesion as primary. I cannot regard such an indurated lesion as a gumma.

Book Reviews

Handbuch der Haut und Geschlechtskrankheiten. Edited by J. Jadassohn. Volume XII, part 1: **Tropische Dermatosen, juxtaartikuläre Knoten, Rattenbisskrankheit.** Price, 168 marks; bound, 176 marks. Pp. 857. Berlin: Julius Springer, 1932. Volume XII, part 2: **Geschwülste der Haut.** Price, 134 marks; bound, 142 marks. Pp. 700. Berlin: Julius Springer, 1932. Volume XII, part 3: Price, 248 marks; bound, 257 marks. Pp. 1200. Berlin: Julius Springer, 1933.

Part 1 of volume 12 is a book of nearly 900 pages and is devoted chiefly to tropical diseases of the skin. It has chapters on frambesia; gundu; tropical phagedena; leishmaniasis; the exanthems and other pictures of the skin in tropical diseases; verruca peruviana; dermatomycosis in the tropics; tropical blastomycosis; animal parasites of the skin in tropical countries, and the skin and helminths. The work also considers the common diseases of the skin in the colored races, and juxta-articular nodes and rat-bite fever, which are sandwiched in between other subjects without any apparent logical association. Juxta-articular nodes are considered in two articles in two different parts of the book. The subjects are not considered as fully as is usual in this encyclopedia, and the discussions are of unequal value, but the whole is a valuable summary of tropical dermatoses.

Parts 2 and 3 are a monumental work on cutaneous tumors and leave little to be desired. The various subjects are considered by men who can write authoritatively on their subjects, and the volumes cover the field in every aspect, from history to bibliography. As examples: The many interesting questions involved in the subjects of warts and condylomas are given 175 pages by Dr. W. Freudenthal and Dr. R. Spitzer; and the consideration of epithelioma by Prof. S. C. Beck and Dr. Lang is in itself a volume of 345 pages. These two volumes are an invaluable storehouse of knowledge on the subject of tumors of the skin.

The Merck Manual of Therapeutics and Materia Medica. Sixth edition. Price, $2. Pp. 1379. Rahway, N. J.: Merck & Co., 1934.

This is a handy reference book, covering the whole domain of therapeutics and materia medica. It is a reliable summary of therapeutics and materia medica, which must be valuable to any one in refreshing the memory and which the dermatologist may well have on his desk. Nowhere else, in the reviewer's knowledge, is so much information on these subjects so conveniently available. That it has proved a useful volume is shown by the fact that six editions have been issued, and it now contains more than 1,350 pages. Of these, 1,200 pages in this edition are devoted to therapeutics, which is fortunately under the editorial supervision of Dr. Bernard Fantus of the University of Illinois, who to those who know him is easily first in his knowledge of this subject and who combines with this exceptional knowledge profound scholarship and ripe experience in the practice of medicine.

Directory of Dermatologic Societies *

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

W. R. Jaffrey, President, 64 Hughson St., S., Hamilton, Ont.
Basil Bowman, Secretary-Treasurer, 408 Medical Arts Bldg., Hamilton, Ont.
Place: Montreal, Quebec. Time: May 4, 1935.

Royal Society of Medicine, Section of Dermatology

Henry MacCormac, President, 23, Wimpole St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Jeffrey C. Michael, Chairman, 1215 Walker Ave., Houston, Texas.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Atlantic City. Time: June 10-14, 1935.

American Dermatological Association

Charles M. Williams, President, 114 E. 54th St., New York.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry F. Anderson, President, 1610, 20th St. N.W., Washington, D. C.
Joseph V. Kennedy, Secretary, 1835 Eye St., Washington, D. C.

Central States Dermatological Association

Joseph Brumberg, President, 528 Delaware Ave., Buffalo.
William F. Hoover, Secretary, 333 Linwood Ave., Buffalo.
Place: Buffalo. Time: 1934.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City.
Robert E. Jameson, Secretary, 1014 First National Bank Bldg., Davenport, Iowa.

New England Dermatological Society

Rudolph Jacoby, President, 270 Commonwealth Ave., Boston.
J. Harper Blaisdell, Secretary, 45 Bay State Road, Boston.

Southern Medical Association, Section on Dermatology and Syphilology

Thomas W. Murrell, Chairman, 17 E. Grace St., Richmond, Va.
C. C. Dennie, Secretary, Professional Bldg., Kansas City, Mo.
Place: San Antonio, Texas. Time: November, 1934.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Ernest K. Stratton, Chairman, 490 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
J. J. Saxton, Secretary, 205 Zack St., Tampa.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, Maison Blanche Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

George M. MacKee, Chairman, 200 W. 59th St., New York.
Lopo de Mello, Secretary, Medical Arts Bldg., Syracuse.

Medical Society of the State of Pennsylvania Section on Dermatology

Robert L. Gilman, Chairman, 1930 Chestnut St., Philadelphia.
Fred M. Jacob, Secretary, 7026 Jenkins Arcade Bldg., Pittsburgh.

Michigan State Medical Society, Section on Dermatology and Syphilology

A. R. Woodburne, Chairman, 26 Sheldon Ave., Grand Rapids.
G. Warren Hyde, Secretary, 2501 W. Grand Blvd., Detroit.

Minnesota Dermatological Society

D. D. Turnacliff, President, 407 Medical Arts Bldg., Minneapolis.
L. H. Winer, Secretary, 522 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma Dermatological Association

C. L. Brundage, President, 1200 N. Walker St., Oklahoma City.
M. M. Wickham, Secretary, 720 Symmes St., Norman.

Texas Dermatological Society

C. F. Lehmann, President, 303 E. Houston St., San Antonio.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Louis Chargin, Chairman, 1 W. 85th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Arthur Persky, President, 1750 Ocean Parkway, Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo-Rochester Dermatological Society

Earl D. Osborne, President, 471 Delaware Ave., Buffalo.
Richard L. Saunders, Secretary, 33 Linwood Ave., Buffalo.

Chicago Dermatological Society

James H. Mitchell, President, 25 E. Washington St., Chicago.
Max S. Wien, Secretary, 104 S. Michigan Ave., Chicago.

Cincinnati Dermatological Society

Samuel Goldblatt, President, 3208 Colerain Ave., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

R. E. Barney, President, 1021 Prospect Ave., Cleveland.
E. W. Netherton, Secretary, 2020 E. 93d St., Cleveland.

Detroit Dermatological Society

Clyde K. Hasley, President, 1553 Woodward Ave., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Moses Scholtz, Chairman, 1930 Wilshire Blvd., Los Angeles.
Nelson P. Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.

Manhattan Dermatologic Society

Louis B. Mount, Chairman, 256 State St., Albany, N. Y.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

Alberic Marin, President, 1414 Drummond St., Montreal, Canada.
Paul Poirier, Secretary, 2073 St. Denis St., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Ray H. Rulison, Chairman, 145 E. 54th St., New York.
E. William Abramowitz, Secretary, 853, 7th Ave., New York.

New York Dermatological Society

Fred Wise, President, 200 W. 59th St., New York.
R. H. Rulison, Secretary, 145 E. 54th St., New York.

Omaha Dermatological Society

J. W. Hellwig, Chairman, 1319 Farnam St., Omaha.
Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

Philadelphia Dermatological Society

Robert L. Gilman, Chairman, 1930 Chestnut St., Philadelphia.
Vaughn C. Garner, Secretary, Greene and Coulter Sts., Philadelphia.

Pittsburgh Dermatological Society

Bernhard A. Goldmann, President, Jenkins's Arcade, Pittsburgh.
J. Cavanaugh, Secretary, 28 Market St., Youngstown, Ohio.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

H. J. Templeton, President, 3115 Webster St., Oakland, Calif.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

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